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THE

AMERICAN JOURNAL

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NOVEMBER, 1913

ORIGINAL ARTICLES

THE CLINICAL FEATURES OF CASES OF SUBACUTE BACTERIAL ENDOCARDITIS THAT HAVE SPONTANEOUSLY BECOME BACTERIA-FREE.[1]

By E. Libman, M.D.,

NEW YORK.

At the meeting of the Association of American Physicians in 1912, the writer[2] presented a paper on the results of a study of the endocardial lesions found in cases of subacute bacterial endocarditis (chronic malignant endocarditis, chronic infectious endocarditis, chronic ulcerative endocarditis, endocarditis lenta). After describing these lesions he presented evidence that the bacteria in such cases could spontaneously disappear from the lesions and that the lesions could heal in part or entirely. It was shown that the healing of the lesions was not necessarily accompanied by recovery from the clinical standpoint. There are two reasons for this. In the first place the healing of the lesions leaves fibrous and calcareous tags or masses, which interfere with the usually already improper functioning of the valves and the musculature of the heart, and which may give rise to embolic phenomena. In the second place so much injury may be done to the kidneys and the blood-forming organs that although the bacteria disappear the damaged tissues cannot functionate to the extent necessary for the preservation of life.

In the paper referred to there were briefly presented notes on eleven cases, concerning which there was no doubt that the patients

[1] Read at the meeting of the Association of American Physicians, Washington, D. C., May 8, 1913

[2] Libman, Amer. Jour. Med. Sci., September, 1912, cxliv, 313; Trans. Assoc. Amer. Phys., 1912, xxvii.

had suffered from subacute bacterial endocarditis and had spontaneously become bacteria-free. In three of these cases (these were the earliest cases) the condition was not suspected clinically, and the diagnosis was established by the evidence accumulated by a study of the postmortem material. In the other cases the diagnosis was made from the clinical features and proved by bacteriological and pathological investigations. The presence of the embolic glomerular lesions in the kidneys, described by Loehlein, and later by Baehr[3] and Gaskell, we found to be pathognomonic of the existence of subacute bacterial endocarditis when due to the cocci usually found in such cases. In those cases which were due to the influenza bacillus, such lesions were not found. As these cases are quite infrequent, this is not evidence that such lesions cannot be produced by subacute or chronic endocarditis due to this organism.

It is my present purpose to give a short review of the clinical features of the bacteria-free cases that we have observed up to to the present time. As it would not be possible, except in monographic form, to discuss these cases in detail, only certain important points will be mentioned. There will be appended a short description of the clinical course of each of the cases which were utilized in the course of the study.

In the earlier paper the following description was given of the clinical course of the cases seen up to that time:

1. They may develop a nephritis and die of uremia.

2. They present the picture corresponding to what we have been wont to call chronic endocarditis with fever (that is, they have a valvular lesion, more or less fever from time to time, usually low, occasional petechiæ, occasional joint symptoms, and embolisms). Some of these cases resemble cases in which bacteria are demonstrable in the blood. Some are pale, others more or less pigmented.

3. Some of the cases present a complex that appears to have been entirely overlooked. The striking feature is a peculiar diffuse brown (sometimes quite dark) color of the face. The rest of the body may show some pigmentation. There is evidence of a valvular lesion, there is more or less anemia, usually a palpable spleen, and usually also tenderness of the sternum. The patients feel weak and do not sleep well. Petechiæ occasionally occur. There is fever from time to time, usually low. Erythrocytes are found in the urine in some of the cases. The subsequent history of such cases is not yet known; one case died with symptoms of cerebral embolism. The important feature of these cases is the curious change in the color of the face. Since I have observed it in bacteria-free cases, I have looked for it in cases in the bacterial

[3] Amer. Jour. Med. Sci., September, 1912, cxliv, 327.

stage, and, to my surprise, I find that while the faces of most of the cases are sallow, or of a rather white color, some develop a certain amount of brown or café-au-lait color.

4. They may go on with more or less anemia, and suffer from that and from decompensation.

In discussing the splenic enlargement which occurs in the bacteria-free as well as in the bacterial stage, I suggested that from observations made several years before, I had reason to believe that a case would occasionally be found in the bacteria-free stage in which marked enlargement of the spleen might be a very conspicuous feature of the case. I suggested that when such a case did come under observation, it might be regarded as a case of Banti's disease plus chronic valvular disease, and that it might not be recognized that the case was really one of subacute bacterial endocarditis in the bacteria-free stage, with marked enlargement of the spleen as the most conspicuous feature. During the last year I saw a case which showed that such a clinical picture is possible. A description of it is appended (Case XXI).

I have given the classification which I described in the paper published last year, because it is the basis of my present classification. After describing the mode of onset, the symptoms, and the termination of the cases in the bacteria-free stage, I shall show in what way I have found it necessary to modify the classification.

The remarks which follow are based on a study of 21 cases of subacute bacterial endocarditis in the bacteria-free stage; 4 of the cases are still alive. Postmortem examinations were made in 17 of the 18 cases that succumbed, and in all there was ample proof from the clinical, bacteriological and pathological studies that we were dealing with the disease under discussion. In the course of the investigations, 1 case was encountered which was suspected of being in the group, but there was not sufficient evidence present at the postmortem examination to corroborate the clinical suspicion. This case is mentioned among the appended notes, but is not described in detail. It will be of service on another occasion when the question of differential diagnosis is taken up. Up to May, 1910, the writer had observed 43 cases of subacute bacterial endocarditis.[4] Since that time he has made more or less comprehensive studies of 82 more cases, the entire number being 125. Of the 82 cases seen since May, 1910, 18, or over one-fifth, were in the bacteria-free stage (1 case became bacteria-free under observation, Case VIII). The writer is convinced that a careful study of all the cases of chronic valvular disease seen at the hospital during that period would have resulted in unearthing a larger number of cases. It is only by a careful scrutiny of all cases supposed to be instances of uncomplicated chronic valvular disease that one becomes im-

[4] Cf. Libman, Amer. Jour. Med. Sci., October, 1910.

pressed with the frequency with which patients are found suffering from chronic valvular disease plus the bacteria-free stage of subacute bacterial endocarditis.

We will now proceed to a review of some of the clinical features of the disease:

Duration. This is difficult to estimate, as most of the cases were not seen in the bacterial stage, and therefore one can have no idea of the length of the bacteria-free periods. In Case VIII, in which influenza bacilli were found for almost two months, the later bacteria-free period was about four months. There is sufficient evidence to show that the bacteria-free period may last for two and a half years, as in Case XIII. In two cases there was a history of the presence of cutaneous tender nodules three (Case XX) and three and a half years (Case XIII) before death. It is to be remembered that there are a few records in the literature of cases in which patients became bacteria-free under observation and remained well except for the presence of the previously existing valvular lesion. But the period of observation in these cases was not very long when the cases were reported, and no later reports have been issued which state whether the patients developed any of the special features to which we have drawn attention as occurring in the bacteria-free stage.

Previous History. In one case there was a history of scarlet fever at an early age. In a number of cases there was a history of previous attacks of rheumatism and of the establishment of a valvular lesion. In some cases the patients had suffered for a longer or shorter time from palpitation, dyspnea, pain in the precordial region, and cough with or without expectoration; at times the sputum was hemorrhagic.

In a few of the cases there was a history of an attack of fever, pains in the joints, palpitation, and dyspnea a number of months before the development of the symptoms for which the patient came under observation. It is proper to suspect that these attacks in some instances represent the bacterial stage of the disease. A critical analysis of the data bearing on this point will be submitted at another time.

Mode of Onset. In most of the cases the early symptoms were cardiac in nature. There was dyspnea, palpitation, and cough with or without hemorrhagic expectoration. With these symptoms there might or might not be chilly sensations, fever, sweats, joint pains, and swelling of the legs. In one case severe pain in the thigh was the first symptom (due to an embolic aneurysm of the femoral artery). In another a severe pain in the sacral region was the prominent early symptoms (this is at times observed also in the bacterial stage of the disease). Vomiting associated with headache and dizziness was the initial symptom-complex in a couple of cases; in one case epistaxis, and in another purpura first appeared. Frequency

of urination was a striking symptom that appeared early in two cases.

Fever. The temperature in the bacteria-free cases does not run as high as in the bacterial cases. It may be high in cases that are seen, apparently, shortly after the bacterial stage has ended, or if complications develop or an intercurrent disease. Embolisms may cause marked rises of temperature, and at times chills, even though there be no bacteria in the pieces thrown off from the valves. In many cases the temperature is practically normal during almost the entire period of observation.

Valvular Lesions. In every one of the cases there was evidence of an organic lesion of the mitral or aortic valve, often of both. As a rule no new murmurs developed during the disease.

Renal Phenomena. This subject is so important in connection with the symptomatology of the bacteria-free stage of subacute bacterial endocarditis that it is possible to give only the shortest account of our observations. Macroscopically, hemorrhagic urine usually occurs either when the case comes under observation shortly after the bacterial stage is ended (as made apparent by the clinical pictures or by the study of the age of the vegetations found in the heart) or as the result of gross embolic lesions of the kidney. Erythrocytes in small numbers are found in the urine in a number of the cases, but not with the regularity or persistence with which they are found in the bacterial stage of the disease.

Albumin and casts are found in some of the cases from time to time. In others there is definite evidence of a more or less marked progressive disease of the kidney. In this latter group of cases there are two types. In the one there is passed a subnormal, normal, or increased quantity of urine of a normal or subnormal specific gravity, albumin and formed elements being more or less conspicuously present. In the cases of the second type there is passed a large amount of urine (up to 2700 c.c.), with a high specific gravity (up to 1028 or 1032), and this may occur even when there are present but a few formed elements and only a trace of albumin. This second clinical type of renal disturbance has not, as far as the writer knows, been previously described. The relationship of the clinical phenomena and the pathological lesions is worthy of a special study.

Symptoms due to renal insufficiency were prominent in a number of cases; in some they dominated the clinical picture. In one case (Case III) the examination of the fundus revealed edema of the optic disks and retina. As will be seen later, renal insufficiency was the main cause of death in a comparatively large number of cases.

Blood Changes. In the cases in which examinations were made (and they were made in nearly all) there was found a more or less marked anemia, always of the secondary type. The hemoglobin

in some cases was as high as 65 per cent., and in others as low as 35 or even 20 per cent. There was a tendency to progressiveness in the anemia in many of the cases. Nucleated erythrocytes were never found. The bone-marrow of the femur was examined in two cases, and was found to be dark red in color, and to show typical regenerative changes. In a third case the tibia was examined and fatty marrow found.

When the anemia was profound it was plainly revealed by the color of the skin and mucous membranes, and by a general edema most marked in the lower limbs.

The leukocytes were usually not increased in number except when complications ensued. In some cases the number diminished during the course of the disease (to 4000 at times). The polymorphonuclear cells were either normal or moderately increased (barring periods during which there were complications). In a few cases they diminished during the progress of the disease (in one case to 36 per cent.).

Splenic Enlargement. The spleen was palpable in all the cases except four. At times it was enormously enlarged. In all the cases but one of those in which the spleen was not palpable it was found enlarged at the postmortem examination, at times very much so. In a large percentage of the cases the Malpighian bodies in the spleen were conspicuously enlarged and, microscopically, hyperplastic.

Petechiæ. These were found at one time or other in 13 cases. They were located in the mucous membranes (especially the conjunctivæ) and the skin. As a rule few were found as compared with the number seen in cases in the bacterial stage.

Purpura. This was noted in three cases. In one it was the main symptom for two months before the patient came under observation. In another case it occurred repeatedly throughout the course of the disease.

Tender Cutaneous Nodules. These were found in only three cases. In two they persisted close up to the time of the fatal termination. One of these two patients had had these lesions for three years, and one for three and a half years.

Sternal Tenderness. This symptom, as the writer stated last year,[5] seems to be more marked in the bacteria-free stage than in the bacterial stage. It was found in all of the cases in which it was looked for. In one case the tenderness of the lower sternum was so marked that it was elicited by the lightest tap. The long bones were usually not found tender.

Sweats and Loss of Weight. These symptoms were not nearly as marked as in cases in the bacterial stage. In only a few cases is there a note of profuse perspiration. That loss of weight should not be a prominent symptom is evident from the fact that many

[5] Trans. Assoc. Amer. Phys., 1912.

of the cases have comparatively little fever as compared with cases in the bacterial stage.

PIGMENTATION. The brown color of the face was noted as a striking symptom in nine cases. In some of these it increased under observation. A few of the anemic patients whose faces were at first white, later developed a more or less marked café-au-lait tint. This has also been observed by the writer, as stated in a previous publication, in the bacterial stage, but the development of a marked brown color he has seen only in cases in the bacteria-free period.

PAINS. The only pains that occurred with any frequency were joint pains. These occurred particularly in the cases in which purpura was a symptom. Reference has already been made to the case in which pain in the sacrum was a marked feature. Pains due to various complications need no discussion here.

ANEURYSMS. Apart from the occurrence of aneurysms of the mitral valve, the septum membranaceum, and the sinuses of Valsalva, which produced no recognizable symptoms, there was encountered once an embolic aneurysm of the femoral artery. The aneurysm had ruptured into the soft parts and had eroded the bone. The patient was sent into the surgical service of the hospital with a diagnosis of osteomyelitis, because of the rapidly developing large tender swelling, the fairly high temperature, and the high leukocyte count with polynucleosis. Because of the presence of a valvular lesion, a large spleen, and a marked anemia, I suspected that we were dealing with a case of subacute bacterial endocarditis. Further observation proved that this view was correct. The post-mortem examination corroborated the clinical opinion; the lesions were practically bacteria-free, and for the main part organized. This was in keeping with the fact that the three blood cultures made in the case gave a negative result.

CARDIAC SYMPTOMS. These can be classed in two groups. We must consider first the subjective and objective symptoms due to the valvular lesion as such. Here we include the palpitation, pains in the chest, dyspnea, cough and expectoration, congestion of the viscera, edema of the legs, and hemorrhagic infarction of the lungs.[6] All these symptoms may occur in any case of valvular disease.

In the second group we include the embolisms, petechiæ, purpura,[7] embolic aneurysms, and tender cutaneous nodules; this second group of symptoms occurs when there are friable masses on the valves of the heart or on the wall. They are therefore common events in cases of subacute bacterial endocarditis in the bacterial or bacteria-free stage, and may well be called endocarditic symp-

[6] These are due oftener than is generally supposed to thromboses in veins of the lower extremities or of the pelvis.

[7] This could, of course, at times be due to a hemorrhagic diathesis.

toms. Cerebral embolism seems to be as frequent an occurrence in bacteria-free as in bacterial cases.

JOINT SYMPTOMS. These are much less common than they are in the bacterial stage. There may be joint pains or joint swellings, or both. Occasionally, as stated above, purpura is also present. The joint swellings are, as a rule, not marked, and are quite transitory. The writer does not remember having seen a joint that was tender or over which the skin was red.

CAUSE OF DEATH. The cause of death can be fairly definitely stated in 16 of the fatal cases: In 3 it was due to cerebral embolism, in 4 to uremia, in 2 to the progressive anemia and an intercurrent pneumonia, in 1 to uremia, embolism, and pneumonia, in 1 to pneumonia, in 3 to cardiac insufficiency, in 2 to progressive anemia, with concomitant cardiac weakness. To put the matter in another way, it may be said that cerebral embolism was a determining factor in 4 cases, uremia in 5 cases, intercurrent pneumonia in 4 cases, anemia in 4 cases, and cardiac insufficiency (unaccompanied by profund anemia) in 3 cases.

The important role played by the progressive anemia, the nephritic changes, the presence of vegetations on the valves, and the improper functioning of the valves and musculature of the heart is thus made very clear.

The lesions found in the heart in all the cases were, in the main, of the same type as those described in the writer's earlier paper on this subject. In two cases atypical lesions were found, the main feature of which was a peculiar worm-eaten appearance of the mitral valve, which in both instances was the seat of an old mitral stenosis (Cases XIII and XX). In one of these two cases the glomerular lesions were of a diffuse type and the typical embolic lesions were not present. The clinical history was, however, quite typical, and the characteristic tender cutaneous nodules were seen by the writer.

GENERAL GROUPING OF THE CASES. From the description which we have just given of the symptomatology of the disease under consideration it might appear that most of the cases look quite alike clinically. But while it is true that petechiæ, sternal tenderness, a palpable spleen, and a more or less marked anemia occur in most instances, the cases can be grouped according to certain features that particularly impress the observer. In the earlier part of this paper the writer quoted the classification of the cases that he attempted to make and which he presented last year, and he also drew attention to the occasional occurrence of an unusual enlargement of the spleen. The study of the additional cases seen since then, in conjunction with a review of the earlier cases, leads him to describe five prominent features, one or more of which may be found in a certain case, and characterize the case rather than describing four or five groups; for he has found there are cases

that belong to more than one of the groups which he described last year.

The five prominent features which may be found are:

1. Marked progressive anemia.
2. Brown pigmentation of the face.
3. Marked evidence of renal disease.
4. Marked enlargement of the spleen. The spleen may be so enlarged that the case may be considered a case of chronic valvular disease associated with Banti's disease.
5. Phenomena due to the vegetations present on the valve. These are what I term endocarditic symptoms. They consist of more or less elevation of temperature occurring from time to time, petechiæ, occasional joint symptoms, and embolisms.

Whenever any of these clinical features are found in a case of chronic valvular disease it is of the greatest importance, for it draws attention to the possibility that the case is one of chronic valvular disease plus subacute bacterial endocarditis in the bacterial or bacteria-free stage.

Afebrile or nearly afebrile periods of fair duration (several weeks) or negative results of blood-cultures would help make the differentiation between the two stages.[8] The diagnosis from certain cases of acute rheumatic infection of a valve previously the site of disease, and from some other conditions may present difficulties. The writer will not discuss this question, as it is his purpose at the present time to describe clinical features and not differential diagnosis. All he wishes to state now is that studies made by Dr. D. J. Kaliski and Dr. P. Aschner have not demonstrated the value of complement fixation tests as an aid in the diagnosis of bacteria-free cases.

In the appended description of our cases, summaries are given which show which of the five important features of the bacteria-free cases occurred in each. A few examples will, however, be of interest here:

Case I. Pigmentation; endocarditic symptoms.

Case III. Nephritic symptoms.

Case V. Endocarditic symptoms; progressive anemia.

Case VI. Endocarditic symptoms; intense anemia; pigmentation.

Case XV. Pigmentation.

Case XXI. Marked splenic enlargement; progressive anemia; renal symptoms.

Description of Clinical Course of Cases. In the following notes there will be presented a concise description of all the cases

[8] It is an interesting fact that in cases of subacute bacterial endocarditis in the bacterial stage, bacteria can practically always be found in the blood if the temperatures are not elevated a great deal. It is in the cases with high temperatures and with very marked oscillations that one fails at times to obtain bacteria in the blood cultures although the bacteria are present in enormous numbers in the vegetations in the heart.

of subacute bacterial endocarditis in the bacteria-free stage that the writer has observed. As the cardiac lesions were described rather fully in the paper presented before the Association last year, and as it is his purpose at another time to publish an account of these lesions in greater detail, he will, in the descriptions of the cases, refer to the postmortem findings in as brief a manner as possible. The renal lesions will also not be described at the present time, as they will form the basis of another communication. It is sufficient to state that in nearly all the cases the embolic glomerular lesions, which are characteristic of the disease (except when due to the influenza bacillus), were present. In a few cases these embolic lesions were associated with other diffuse glomerular lesions. In a few cases only diffuse lesions of the glomeruli were present. These lesions will be described at another time. In the few cases in which embolic lesions were not present, there was sufficient evidence present clinically (tender cutaneous nodules) or at the postmortem examination to put the cases into the group which the writer has termed subacute bacterial endocarditis in the bacteria-free stage.

A perusal of the following notes will show that the writer has included four patients who are still alive, all of whom are in quite good condition. Although the absolute evidence of the fact that they belong in this group is not forthcoming, the cases are so typical clinically and correspond so closely to other cases in which the clinical diagnosis was proved correct by postmortem examination that it seemed desirable to include them.

Case I.—Observed from July 2, 1905, to August 6, 1905. Three blood-cultures were made, with negative results. There was a previous history of scarlet fever at the age of two years; pains and redness of the joints during the last winter. Onset one month before admission, with cough and expectoration, cardiac palpitation, dyspnea, pain in both knees, which were red and not swollen. The heart showed evidences of an aortic lesion. The face was markedly pigmented. The spleen was palpable and petechiæ were present. An embolic aneurysm of the iliac artery developed. The patient passed large amounts of urine, up to 2000 c.c. a day, containing a moderate number of leukocytes and hyaline casts. The leukocyte count varied from 6200 to 9200; hemoglobin, 65 per cent., later 61 per cent. The temperature rose at the highest to 101° or 102°, except just before the embolism occurred, due to which the aneurysm developed; at that time the temperature was 104°. The cause of death was apparently a cerebral embolism. Postmortem examination revealed a healed clacareous bacteria-free lesion[1] of the aortic valve, with an aneurysm of the mitral valve and fibrous lesions of the chordæ tendineæ. The spleen was

[1] This means that the cultures from the centre of the vegetations showed no bacteria, and that smears made from crushed vegetations also showed no organisms.

large and showed marked hyperplasia of the Malpighian corpuscles and one infarction. In the kidney there was an embolic aneurysm.

SUMMARY. The main features in this case were pigmentation and endocarditic phenomena (development of non-bacterial embolic aneurysms).

CASE II.—Observed from May 1, 1907, to October 3, 1907. There were two blood-cultures, with negative results. There had been cardiac palpitation and dyspnea for six months. For two months prior to admission, attacks of purpura, and for five weeks edema of the legs, were present. The cardiac lesion was apparently aortic insufficiency. The spleen was palpable just below the free border of the ribs and petechiæ were present. Perspiration was a marked feature. The urine varied in amount from 750 to 850 c.c. Specific gravity ranged from 1008 to 1012; erythrocytes were present, also hyaline and hyalogranular casts. Blood examination at first showed 5200 leukocytes, 53 per cent. hemoglobin, and 3,040,000 erythrocytes. Later the leukocyte counts varied from 4000 to 7000; the polymorphonuclear count was as low as 41 per cent., except a short time before death, when it was 68 per cent. The hemoglobin dropped to 38 per cent. The temperature was usually around 100°, occasionally 101°, except when an embolism occurred or when a purpuric rash developed. Death was due to cerebral embolism. The autopsy showed a calcareous lesion of the aortic valve and an aneurysm of the membranous septum. The spleen was almost twice the normal size, contained old and recent infarctions, and the Malpighian bodies were prominent. Areas of softening were found in the brain.

Summary. The important features of this case were endocarditic phenomena (embolisms and purpura), the marked enlargement of the spleen, the urinary phenomena, progressive anemia, and lymphocytosis.

CASE III.—Observed from November 9, 1905, to May, 1906, and again from October 3, 1909, to November 3, 1909. There was one blood-culture, with negative result. A history was obtained of rheumatism occurring two years before the date of the first admission. During the first stay in the hospital there were joint symptoms and a pericarditis. Hemoglobin was 86 to 90 per cent., but progressively dropped to 65 per cent. The temperature was at first up to 103°, afterward practically around normal, except with occasional rises to 101° or 101.2°. The quantities of urine varied from 620 to 1600 c.c. The specific gravity varied between 1008 and 1028, being usually around 1010 to 1020; there was present a faint trace of albumin, and occasional hyaline and hyalogranular casts. The spleen was not palpable. There were evidences of mitral insufficiency. On admission the second time the patient gave a history of having developed edema of the legs five weeks before. Ophthalmoscopical examination showed marked edema

of the optic disks and surrounding retina. Hemoglobin dropped to 36 per cent. Urine quantity varied at first from 1300 up to 3000 c.c., and later dropped to 330 c.c. At the time of the second admission the urine contained a trace of albumin, numerous hyaline and granular casts, and leukocytes; later it was reddish brown in color, contained a heavy trace of albumin and numerous erythrocytes. The patient died of uremia. At autopsy there was found a fibrous lesion of the wall of the left auricle and fibrous and calcareous lesions of the chordæ tendineæ. The spleen was one and a half times the normal size.

Summary. The main features of this case were the progressive anemia and the renal phenomena.

Case IV.—Observed from April 24, 1910, to May 9, 1910. There was one blood culture, with negative result. The patient had been dyspneic for one year. For two weeks there was vomiting, headache, and dizziness. There was evidence of mitral and aortic insufficiency; the spleen was palpable. There were no petechiæ. The patient looked anemic. Hemoglobin was 60 per cent.; leukocytes, 13,000; polymorphonuclears, 65 per cent. The urine varied in specific gravity from 1010 to 1013; there was present a faint trace of albumin; occasional hyaline casts, erythrocytes, and granular casts. The temperature was never over 102°, usually between 99° and 100°. The patient died of uremia, cerebral embolism, and a terminal pneumonia. The autopsy showed old pericardial adhesions and a lesion of the wall of the left auricle and of the chordæ tendineæ, which was almost entirely healed. The spleen was one and a half times the normal size, and contained infarctions.

Summary. Renal phenomena, old pericarditis, moderate anemia.

Case V.—Observed from July 14, to October 8, 1910. There were three blood cultures, with negative results. There was a history of articular rheumatism at the age of six years, and of palpitation and dyspnea since that time. The onset of the present illness occurred ten weeks before admission to the hospital, with pain in the thigh, swelling, and limping, all this being due to a ruptured embolic aneurysm of the femoral artery. The heart showed evidences of mitral and aortic insufficiency. The spleen was large (the spleen was particularly large in view of the fact that the boy was sixteen years of age and much undersized). There was a café-au-lait color to the face. The urine at first showed a specific gravity of 1020, later 1004 up to 1020; there were present erythrocytes and hyalogranular and granular casts. The blood count showed 15,200 leukocytes; 65 per cent. polymorphonuclears and a hemoglobin content of 20 per cent.; later the leukocyte count was 8400; polymorphonuclears 36 per cent., and the hemoglobin dropped to 17 per cent. The temperature was usually up to 102°. Death occurred from progressive anemia and a terminal

pneumonia. The autopsy showed lesions of the mitral valve, chordæ tendineæ, and auricular wall, most of which were healed. In one part of the lesion there were found a few poorly staining cocci. The spleen weighed 510 grams (17 ounces); Malpighian bodies large.

Summary. Embolic aneurysm; marked splenic enlargement; renal phenomena; progressive anemia.

CASE VI.—Case observed from June 26, 1911, to April, 1912. There were nine blood-cultures, with negative results. There was a previous history of rheumatism. The onset occurred three months before admission, with increase of a previously existing palpitation and dyspnea. There was frequent urination. The heart gave evidence of an aortic lesion. There was marked pigmentation of the face. The spleen was palpable. Numerous petechiæ occurred often. There were hemorrhages from the gums. There were tender nodes on the hands and feet on August 30 and October 4, and even as late as March 1. The lower sternum became distinctly tender under observation. The urine was at first grossly bloody, later erythrocytes were found microscopically from time to time. The specific gravity varied from 1020 to 1022; the amounts of urine were from 1100 to 2400 c.c. The blood-examination showed a hemoglobin content of 39 per cent. at first; this then dropped somewhat lower, and a transfusion was done and the hemoglobin brought up to 55 per cent. It then rose to 61 per cent., but later dropped again. Leukocyte count was 10,400; polymorphonuclears, 81 per cent. The temperature was at first 101° to 102°, and later was occasionally as high as 101°, except just before crops of petechiæ developed. Death was due to progressive anemia and a terminal pneumonia. At the postmortem examination there were found calcareous and fibrous lesions of the aortic valve and aneurysms of the sinuses of Valsalva. The spleen was one and a half times the normal size; there was marked enlargement of the Malpighian bodies. The bone-marrow of the femur was red, and microscopically there were evidences of regeneration.

Summary. Pigmentation; renal phenomena; progressive anemia; tender nodes present long after the active stage of the disease was passed; hemorrhagic tendency; endocarditic symptoms.

CASE VII.—Period of observation from April 16, 1911, to June 13, 1911. Cultures of the blood were not made during life, but at the postmortem examination the blood was found free from bacteria, as were also the cardiac lesions. There was a previous history of acute articular rheumatism and of cardiac disease. The patient suffered from dyspnea, pain over the heart, cough, and hemoptysis. The present illness began two weeks before the date of admission, with dyspnea, orthopnea, pains about the heart, cough, and expectoration, which was a times hemorrhagic. Examination showed insufficiency of both aortic and mitral valves. Spleen not

palpable. No petechiæ. Urine showed a specific gravity of 1020 to 1026, and contained a trace of albumin. The quantities varied from 1400 to 1900 c.c. The temperature was usually up to 101° or 101.2°, later at one time up to 102°. The patient developed uremia and died suddenly, the explanation of the sudden death being unknown (the writer did not observe this case himself). At the postmortem examination there was found an adherent pericardium and a bacteria-free and partially healed lesion of the chordæ tendineæ, mitral valve, and auricular wall. The spleen weighed 570 grams (19 ounces), and contained infarctions.

Summary. Renal phenomena; marked splenic enlargement.

Case VIII.—Period of observation from July 17, 1911, to October 14, 1911. In this case the first five blood-cultures gave growths of the influenza bacillus, three later ones remained sterile, the first of the latter being taken on September 9. The patient was told two years before the onset of the present illness that he had endocarditis. For eighteen months he had had pain in the ankles and feet, and had lost weight. On admission he complained of throbbing in the head, fever, and weakness. There were evidences of aortic insufficiency and mitral stenosis. At first the spleen was felt two fingers below the free border, and later four fingers below the free border. Petechiæ were present. The specific gravity of the urine varied from 1008 to 1024, later from 1011 to 1020; erythrocytes and hyaline and granular casts were present. Blood-count showed leukocytes, 6800; polymorphonuclears, 75 per cent.; hemoglobin, 64 per cent.; later the hemoglobin was 71 per cent, leukocytes 5800, and polymorphonuclears 42 per cent. The patient left the hospital some time after the blood was bacteria-free, and developed a marked progressive anemia and hydremia. At first the temperature was 104°, later not above 102°. The patient died of progressive anemia and exhaustion. An autopsy was not permitted.

Summary. Influenza bacillus infection; the case later became bacteria-free; progressive anemia; marked enlargement of the spleen.

Case IX.—Period of observation from August 8, 1911, to August 24, 1911. Two blood-cultures were taken, with negative results. The patient had previously been in the hospital from September 24, 1910, to October 15, 1910. On the first admission there was a history that the patient had had rheumatism since he was fifteen years old. Six months before the day of the first admission the patient was taken sick with fever and pain in various joints. He had marked sweats, occasional dyspnea, palpitation, and pain over the heart. The face was of a brownish color. Examination of the heart revealed mitral insufficiency and aortic insufficiency. The spleen was palpable one and a half fingers below the free border. Petechiæ and purpura both occurred. The lower

sternum was distinctly tender. Urine showed a specific gravity of 1018 to 1020, a faint trace of albumin, some hyaline casts, and a few leukocytes. Blood examination at first showed leukocytes, 11,000; polymorphonuclears, 74 per cent.; later blood count showed leukocytes, 6000; polymorphonuclears, 74 per cent. On the day of admission the temperature was 103°, but after that did not rise above 100°. The patient died of cardiac insufficiency and uremia. Postmortem examination showed a bacteria-free calcified and ulcerative lesion of the aortic valve. The spleen weighed 210 grams (7 ounces); old infarctions were present; Malpighian bodies were prominent.

Summary. Pigmentation; endocarditic symptoms.

CASE X.—Period of observation from November 27, 1911, to January 31, 1912. Three blood-cultures remained sterile. Patient was taken sick, three weeks before admission, with dyspnea, cardiac palpitation, and nocturnal frequency of urination. There was marked brown pigmentation of the face. Examination of the heart revealed insufficiency of the aortic and mitral valves. The spleen was not palpable until shortly before death, when it was felt two fingers below the free border of the ribs. Petechiæ were present. The sternum was tender. Urine examination showed a specific gravity of 1016 to 1028, a trace of albumin, and occasional erythrocytes. Quantities of urine varied from 1500 to 2300 c.c. Blood-examination showed leukocytes, 9200; polymorphonuclears, 61 per cent.; later examination showed leukocytes, 7500; polymorphonuclears, 59 per cent.; hemoglobin, 65 per cent. The temperature was often up to 101° at first, and later 100° (except for rises due to an infection of the maxillary antrum and due to an acute otitis media). Death appeared to be due to embolism. Postmortem examination showed bacteria-free lesions of the aortic and mitral valves. The spleen weighed 420 grams (14 ounces), contained infarctions, and the Malpighian bodies were prominent.

Summary. Pigmentation; renal phenomena; embolism. This is one of the cases in which the patient passed large amounts of urine of high specific gravity.

CASE XI.—Period of observation from December 26, 1911, to January 30, 1912. The patient had previously been in the hospital from March 18 to April 15, 1911. Three blood-cultures were taken, with negative results. On the first admission there was cough and palpitation. Petechiæ were present. Temperature 101°, later 100°. Two days before the date of the second admission there was pain in the right forearm, due to embolism of the brachial artery just before its bifurcation. Examination of the heart revealed insufficiency of the aortic and mitral valves. Spleen was not palpable. Petechiæ were present. The sternum was tender. The urine varied in amount from 900 to 1300 c.c., contained albumin and casts, but no erythrocytes. Blood examination showed leuko-

cytes, 11,000; polymorphonuclears, 71 per cent. There is no record of a hemoglobin estimation, but the patient looked anemic. The temperature was at first 102°, later 101°. Death was due to cardiac insufficiency and anemia. At the postmortem examination there was found a bacteria-free healed lesion of the mitral valve and the chordæ tendineæ. The spleen weighed 135 grams (4½ ounces); there were infarctions present; Malpighian bodies were prominent.

Summary. Endocarditic phenomena and anemia.

CASE XII.—Period of observation from December 28, 1911, to December 31, 1911. One blood-culture was taken, with negative result. The patient had previously been in the hospital from March 24, 1905, to April 11, 1905, and from April 20, 1909, to May 1, 1909. There was a previous history of acute rheumatism. During the first two admissions he was supposed to be suffering from chronic endocarditis and rheumatism. At the time of the last admission he had been sick for four weeks, complaining of dyspnea, cough, cardiac palpitation, night sweats, and chilly sensations; he was very pale. There was marked sternal tenderness. The temperature never rose over 101°. The quantity of urine was at first 2700 c.c., and later dropped to 800 c.c. The urine showed a specific gravity of 1025 to 1028, later 1011. Blood-examination showed leukocytes, 10,000; polymorphonuclears, 78 per cent.; hemoglobin, 53 per cent. The patient died of cardiac insufficiency (and secondary renal insufficiency). Postmortem examination showed slight lesions of the aortic valve and marked lesions of the mitral valve, both bacteria-free. The spleen weighed 540 grams (18 ounces); there were infarctions present.

Summary. Moderately marked anemia; renal phenomena; marked splenic enlargement.

CASE XIII.—Period of observation from January 10, 1912, to March 21, 1913. The patient had been at the hospital from January 10, 1912, to March 5, 1912. There were four blood cultures, with negative results. On the first admission to the hospital the patient was suffering from chronic endocarditis, with pulmonary infarctions and a cerebral hemorrhage (as proved by the bloody character of the lumbar puncture fluid, which was obtained at the time). When admitted on January 10, 1912, he gave a history of having had rheumatism eight years before, and since that time frequent attacks of pain about the heart and shortness of breath and also pains in the extremities. Two weeks before admission he was taken sick with a severe pulmonary hemorrhage; he was also suffering from pains in the region of the heart and the left shoulder-joint, and marked weakness. He developed a brown color of the face under observation. There was sternal tenderness present. The cardiac examination revealed a mitral insufficiency and stenosis and aortic insufficiency. He had repeated attacks of purpura. Tender nodes occurred in November, 1912, and the patient stated that he had had them

already three years before. The urine varied in amount from 1700 to 2000 c.c.; the specific gravity was as high as 1030; there were hyaline casts present. During the period of observation there were several attacks of hematuria. Toward the latter part of the disease no erythrocytes were found. There were two attacks of cerebral embolism. The temperature was usually around 99°, except when embolic phenomena or pulmonary infarctions developed. The patient died of cardiac insufficiency. Postmortem examination showed old, bacteria-free, fibrous lesions of the aortic valve and ulcerative and fibrous lesions of the mitral valve, also bacteria-free. The spleen weighed 240 grams (8 ounces) and was scarred from infarctions. The bone-marrow of the tibia was fatty (that of the femur could not be obtained).

Summary. Endocarditic symptoms (embolisms, purpura); pigmentation; renal phenomena; anemia. Special note is to be made in this case of the excretion of large quantities of urine of high specific gravity (the urine contained few or no formed elements when a large amount of concentrated urine was being passed).

Case XIV.—Period of observation from February 1, 1913, until the present time, the patient being alive and in little worse condition than when first seen. There were five blood-cultures made, all with negative results. The main features of this case were pigmentation of the face and exqisite tenderness of the lower sternum. The spleen was palpable at one time, and petechiæ were present in the conjunctivæ during the early part of the observation. The patient is in the hospital at the present time suffering from mitral insufficiency, with attacks of decompensation and acute bronchitis.

Case XV.—Period of observation from September 4, 1911, until the present time, the patient still being alive. One blood-culture was taken, with negative result. This patient suffering from insufficiency of the aortic and mitral valves. He showed marked pigmentation of the face and marked sternal tenderness. The spleen was palpable. He passed large quantities of urine, as high as 2350 c.c. The specific gravity of the urine varied from 1018 to 1027; there was a faint trace of albumin, and erythrocytes were found from time to time. The blood-examination showed leukocytes, 8800; polymorphonuclears, 48 per cent.

Case XVI.—Period of observation from June 4, 1912, until the present time, the patient being still alive. Two blood cultures were made, with negative results. The patient gave a previous history of rheumatism. Two days before admission to the hospital he was taken sick with dyspnea and cardiac palpitation and pain. Face was markedly pigmented, and there was marked sternal tenderness. Petechiæ were found, and there were evidences of mitral insufficiency. He was becoming progressively more pale, and had lost weight. He was passing from 2800 to 2900 c.c. of

urine; specific gravity, 1008 to 1020; some albumin, hyaline and granular casts, and erythrocytes. Blood count showed leukocytes, 10,000; polymorphonuclears, 65 per cent.; hemoglobin, 50 per cent. The temperature ran from 101° to 102°, and once was 103°.

These last three cases appear to the writer to belong with great certainty, to the group under discussion. Cases XV and XVI are both working at the present time; Case XIV is up and about and is staying in the hospital because of the repeated attacks of bronchitis and asthma. These cases are identical with others that were picked out as clinically belonging in the group, and in which the diagnosis was confirmed by postmortem examination.

Case XVII.—Period of observation from August 22, 1912. to August 30, 1912. There was one blood-culture, with negative result. There was a previous history of rheumatism. Five weeks before admission to the hospital the patient complained of headache, fever, and chilly sensations. Examinations of the heart revealed insufficiency of the aortic and mitral valves. The patient appeared anemic. Petechiæ were present, and also marked tenderness of the sternum. Urine examination was practically negative. Blood-examination showed leukocytes, 12,000; polymorphonuclears, 76 per cent. The spleen was palpable two fingers below the free border. The temperature never rose above 100.6°. Death was apparently due to embolisms. Postmortem examination showed bacteria-free old lesions of the aortic and mitral valves. The spleen weighed 540 grams (18 ounces); there was marked hyperplasia of the Malpighian bodies; old infarctions were also present. The bone-marrow of the tibia was found to be red in color and microscopically showed changes found in bone-marrow regeneration.

Summary. Embolic phenomena; marked splenic enlargement; regeneration of the bone-marrow in the femur.

Case XVIII.—This case will not be discussed in detail at the present time. It is the case mentioned above which was suspected of belonging in the group in which there was not sufficient evidence at the postmortem examination to corroborate the clinical diagnosis. It will be described in detail at another time.

Case XIX.—Period of observation from September 16 to the present time, the patient being still alive. One blood-culture was taken, with negative result. This case is only suspicious and cannot be considered to surely be a case in the group. Three years before admission the patient was suffering from dyspnea and palpitation. There was marked brown pigmentation of the face. There was present a stenosis and insufficiency of the mitral valve and insufficiency of the aortic valve. Spleen was palpable. The sternum was distinctly tender. Quantities of urine varied from 700 to 950 c.c.; specific gravity ranged from 1010 to 1026; there was a faint trace of albumin, some leukocytes, and a few erythrocytes. Blood-count showed leukocytes, 7200; polymorphonuclears, 63 per cent.;

erythrocytes, 5,792,000; hemoglobin, 60 per cent. The temperature was practically normal.

Case XX.—Period of observation from September 17, 1912, to October 19, 1912. One blood-culture was made, with negative result. The patient was taken sick, one week before admission, with dyspnea, pain the chest, cough, with bloody expectoration, and swelling of the feet. He stated that he had had lesions that corresponded to the tender cutaneous nodules of subacute bacterial endocarditis on three fingers of the left hand three years before admission. The heart presented evidences of mitral stenosis and insufficiency and aortic insufficiency. The spleen was palpable. The patient looked anemic. The sternum was markedly tender. On September 13 the patient developed tender nodules on the thumb of the left hand, and he had had one on the right hand two weeks before. The quantity of urine passed was as high as 2400 c.c. a day; specific gravity varied from 1012 to 1016; erythrocytes were present, also granular and waxy casts. Blood-count showed leukocytes, 13,400; polymorphonuclears, 58 per cent. There was no record of any hemoglobin estimation, but the patient was evidently anemic. The temperature was up to 102° on September 8; after that it was usually around 99° or 100°, with occasional rises to 100.5°. The patient died of uremia. At the postmortem examination there was found a bacteria-free lesion of the aortic valve, slight in extent, and a more marked lesion of the mitral valve. The spleen weighed 450 grams (15 ounces); Malpighian bodies were prominent.

Summary. Occurrence of tender nodules in the bacteria-free period of the disease; anemia; nephritic condition.

Case XXI.—Period of observation from October 3, 1912, to December 6, 1912. Three blood-cultures were made, with negative results. This was a case which was taken by a number of observers to be one of Banti's disease. The patient, who was aged sixteen years, suffered for four months before admission from epistaxis, weakness, dyspnea, palpitation, swelling of the feet, and increasing pallor. Examination of the heart revealed mitral insufficiency. The spleen was large, being felt four fingers' breadth below the free border. Petechiæ developed during the course of the disease. The color of the face was pale, with a café-au-lait tint. The urine was grossly hemorrhagic from time to time. The specific gravity ranged from 1012 to 1016, and once was 1026. The quantity was from 450 to 1950 c.c. It usually contained erythrocytes and leukocytes, and albumin in fair quantity. Blood examination showed erythrocytes, 2,550,000; hemoglobin, 26 per cent., later 20 per cent.; leukocytes, 6200; polymorphonuclears, 62 per cent.; and later there were, leukocytes 5200, and polymorphonuclears 56 per cent. The temperature at first rose to 103°, later it was only 101°. The patient developed edema of the lower eyelids, vomited repeatedly, and died

in a profoundly uremic condition. At the postmortem examination there were found lesions of the mitral valve and chordæ tendineæ. The spleen weighed 510 grams (17 ounces); the Malpighian bodies were prominent. The cultures made postmortem from the spleen and blood showed an organism corresponding to the coccus generally found in these cases of endocarditis. Spreads made from the lesions in the heart showed absolutely no organisms. It is probable that in this case we are dealing with a case in which the lesions had become bacteria-free or nearly so only a short time before the patient came under observation. The cocci found in the spleen and blood at the time of the postmortem examination may have been thrown out from a few cocci left in some part of the vegetations and from some organ in the body where they had remained in latent condition and had then multiplied after or shortly before death. The fact that no cocci could be found in the vegetations is quite definite proof that the patient was becoming free from the bacterial infection because, as a rule, in all cases in which cocci are found in the blood during life or in postmortem examination the vegetations are full of cocci.

Summary. Marked splenic enlargement; marked renal phenomena; severe anemia; some pigmentation of the face developing under observation.

Case XXII.—Period of observation from December 3, 1912, to December 11, 1912. Only one blood-culture was taken in this case, and in that a typical pneumococcus was found. The case, nevertheless, belongs in the group of cases which are undergoing spontaneous healing, for reasons which will be given when the postmortem findings are discussed. This patient, who was aged fifteen years, stated that she had had, for five years, frequent attacks of cardiac palpitation and dyspnea. The feet were swollen on frequent occasions. Three weeks before admission she was suddenly seized with cardiac palpitation and weakness, and took to bed. She suffered from cough and expectoration, and these symptoms continued until the time of admission to the hospital. For the last eight or nine days before admission she had been jaundiced. Examination of the heart revealed the presence of mitral stenosis and insufficiency and aortic insufficiency. The spleen was palpable and petechiæ were present. The quantities of urine were 500 to 600 c.c.; specific gravity, 1020 to 1022; hyaline and granular casts, and erythrocytes were present; bile was easily demonstrable. Blood-examination showed hemoglobin 48 per cent. The temperature remained around 100° until December 5, when it rose to 105°; on the following days it was up to 103°. This rise of temperature was due to a lobar pneumonia, of which the patient died. At the postmortem examination there was found a bacteria-free lesion of the auricle and mitral valve. The spleen was twice the normal size, and there were old infarctions present. The kidneys showed typical embolic

glomerular lesions, all in the healed state. Because the lesions in the heart were rather old and bacteria-free, and because the embolic lesions in the kidney were all completely healed, and there was practically no temperature up to the time that the pneumonia developed, the writer is of the opinion that the presence of pneumococci in the blood was due to a lobar pneumonia developing in a person who was in the bacteria-free stage of subacute bacterial endocarditis.

Summary. Marked anemia; renal phenomena; terminal pneumonia.

THE NOGUCHI LUETIN REACTION IN SYPHILIS.[1]

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Perhaps there is no disease which is characterized by a greater diversity of pathological lesions or is more protean in its manifestations than syphilis. With a clear history of infection and the existence of tell-tale lesions a definite diagnosis may be made without hesitation. A clear history, however, often cannot be elicited, nor are unmistakable lesions always present. The vague symptoms and signs which indicate the insidious development of internal lesions or the early stages of parasyphilitic conditions may suggest syphilis to the trained syphilographer, but in only too many instances a definite diagnosis is attended with insurmountable difficulties for the average practitioner.

In recent years the laboratory has come to the aid of the clinician in diagnosticating these obscure cases. The Wassermann test is a valuable addition to our armamentarium, but one that is infallible by no means. Certain cases of frank syphilis may never give a positive reaction; the sera of those suffering with leprosy, malaria, yaws, etc., may react positively; treatment may render negative the test despite the persistence of active manifestations; and, finally, in view of the technical knowledge required to properly perform the test, the results are not reliable unless the tests have been made by a trained serologist.

The examination of fresh preparations from active lesions may reveal spirochetes that are diagnostic, but this method is applicable only to lesions which by their objective characteristics alone should suggest syphilis to one who knows the disease. Furthermore, various mouth spirochetes may be confused with the specific treponema of syphilis unless the microscopist be an expert.

As neither clinical nor present laboratory methods are devoid

[1] Published with the permission of the Surgeon General, United States Army.

of possibilities of error, it is obvious that a means of diagnosis that is specific for syphilis, reasonably delicate, easy of application and interpretation, and innocuous as regards the patient, is still needed. The Noguchi luetin test gives promise of fulfilling this need in certain cases.

Stimulated by von Pirquet's demonstration of the cutaneous reaction in tuberculosis, numerous investigators attempted to obtain a similar reaction in syphilis by applying extracts of syphilitic tissues to the skin of luetic individuals. Their results were contradictory. Noguchi[2] states that Neisser and Bruck showed that a reaction similar to that obtained with the luetic extracts could be induced, also, with concentrated extract of normal liver. This peculiar susceptibility of the skin of chronic syphilitics to any form of chemical irritation was designated by Neisser as the state of "Umstimmung." Despite his discouraging results, Neisser expressed the hope that the reaction might be improved by employing an extract of the specific organism of syphilis, free from organic constituents. Improvement along these lines was made possible subsequently by the successful cultivation of Treponema pallidum in pure cultures by Noguchi.[3]

Preparation of Luetin. Noguchi describes the preparation of his luetin as follows: "Pure cultures of several strains of the pallidum are allowed to grow for periods of six, twelve, twenty-four, and fifty days at 37° C., under anaërobic conditions. One set is cultivated in ascitic fluid containing a piece of sterile placenta, and the other in ascitic fluid agar also containing placenta. The lower portion of each solid culture in which a dense growth has occurred is cut out and the tissue removed. The agar columns which contain innumerable spirochetæ are then carefully ground in a sterile mortar. The resulting thick paste is gradually diluted by adding, little by little, the fluid culture which also contains an enormous mass of the pure organisms.

"The dilution is continued until the emulsion becomes perfectly liquid. The preparation is next heated to 60° C. for thirty minutes in a water-bath and then 0.5 per cent. tricresol is added. When examined under the dark-field microscope, numerous dead pallida per field may be seen. Cultures made from this suspension remain sterile and with it no infection can be produced in the testicles of rabbits. The suspension is kept in a refrigerator when not in use.

"In order to ascertain whether the reaction with this suspension might not be due to the introduction of antiseptic culture medium alone, it is necessary to prepare a similar emulsion, with uninoculated media, to be used for control purposes."

[2] A Cutaneous Reaction in Syphilis, Jour. Exper. Med., 1911, xiv, 557.

[3] Experimental Research in Syphilis, with Special Reference to Spirochæta pallida (Treponema pallidum), Jour. Amer. Med. Assoc., 1912, lviii, 1163.

APPLYING THE TEST. Several months ago the writer received from Dr. Noguchi sufficient luetin to apply the test to a series of cases. All my cases were from the out-patient venereal service of the Post Hospital, Fort Leavenworth, Kansas, and the United States Penitentiary, Leavenworth, Kansas. The test was applied to seventy-five persons, seventy of whom at the time were or had been infected with syphilis, while the remaining five individuals were used as normal controls.

The technique recommended by Noguchi was carefully followed in applying the tests. The sterile vials of luetin and control emulsion were thoroughly shaken and the desired amounts of each were then removed from the containers with sterile pipettes and diluted with an equal amount of sterile salt solution. The arms, at the proposed site of inoculation, were thoroughly cleansed with alcoholic sublimate solution. New graduated tuberculin syringes fitted with very fine needles were used in making the inoculations. The syringes were sterilized by boiling, labelled so that no possibility of using the control syringe for luetin emulsion, or *vice versa*, existed, and separate needles were used for each case. The luetin emulsion (0.07 c.c., accurately measured by the graduations on the syringe) was injected intradermically into the skin of the left arm and the control emulsion, in like manner and quantity, was injected into the skin of the right arm. Care was exercised that the inoculations were made very superficially, so as just to raise the epidermis.

In forty-eight cases the reactions were noted daily for a period of ten days, and, subsequently, at periods of two to four days. In the remaining cases the reactions were examined every three to five days. All cases were under observation for from three to five weeks and a note was made of the changes in the individual reactions at each examination.

CHARACTER OF REACTIONS. It was noted that injections of both luetin and control emulsions produced a circumscribed, elevated, blanched swelling about 4 mm. in diameter, similar in appearance to the lesion produced by the bite of an insect in certain persons.

This local swelling entirely disappears in a half hour or so. In positive cases, after twenty-four hours, there is usually more or less inflammatory reaction at the luetin site, manifested by a distinct, circumscribed, indurated, bright red papule. This papule may be surrounded by a hyperemic areola. A reaction may or may not occur at the site of the control injection. When present the control lesion does not exhibit the same degree of induration as the luetin lesion, but otherwise it may appear identical.

At the end of forty-eight hours the luetin papule has become larger, more indurated, and may be surrounded by an inflammatory areola, from which radiate lines of telangiectasis. This marked

inflammatory reaction occurs more commonly between the fourth and seventh days. The control papule, when present, begins to fade in twenty-four hours, and has usually disappeared within three

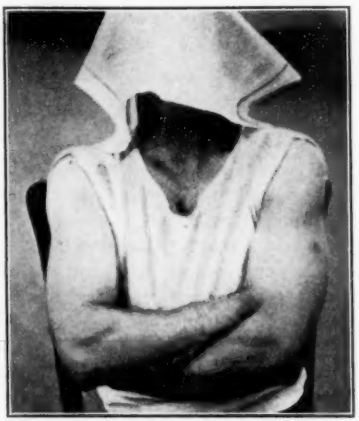

FIG. 1.—Became infected in October, 1911. No active lesions at present. Wassermann positive in June, 1912. The left arm shows a distinct pustular luetin reaction with inflammatory areola, while the right arm shows no trace of the control injection. Photograph taken on the tenth day.

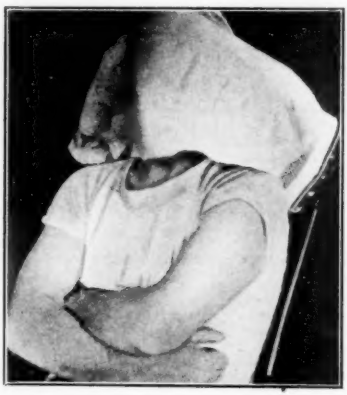

FIG. 2.—Infected in 1908. Treated with mercury and salvarsan. No active manifestations at present. Wassermann negative. Left arm shows a distinct papular luetin reaction. Photograph taken on fifth day.

days. In a few cases, however, beside those evidencing the state of "Umstimmung," more or less discoloration remains at the control site for several days. For this reason I believe that one is

not justified in making a final reading of the reaction before the seventh day. Control lesions which are not due to "Umstimmung" will have disappeared by that time, while positive luetin reactions will still persist, being, as a rule, more marked than on the second or third days. From the second to the sixth or seventh days the reaction becomes progressively intensive. The centre of the papule becomes boggy and deep purplish red in color, and the lesion may be surrounded by an erythematous blush.

As a rule no systemic reaction accompanies the local lesion, but in a few cases there may be complaint of considerable itching and some soreness of the arm. In only one of my cases, was there an appreciable systemic reaction. This patient reported the second day following inoculation with a temperature of 102° F., and complained of brow-ache, malaise, and "soreness all over." His symptoms disappeared entirely in twenty-four hours without treatment.

FIG. 3.—Infected in 1909. Treated with mercury for eighteen months during 1909–10. No active lesions at present. Wassermann strongly positive. The left arm shows the appearance of a luetin pustule on the fifth day.

The papular form of reaction begins to fade about the end of the first week, coincidentally with which desquamation of the epidermis over the papule, and in the more intense reactions for an area around it, occurs. The induration remains for several days after the inflammatory signs have disappeared and its subsidence is followed, in turn, by an area of bluish discoloration which persists in many cases for two or three weeks.

The above description is a brief *resume* of the stages observed in the average papular reaction. In certain cases the lesion be-

comes pustular, usually on the fifth day, followed by rupture of the pustule, as a rule on the seventh day, and crust formation. These pustular reactions seem to bear a rather definite relation to the treatment instituted—a phenomenon that will be discussed later.

A third type of reaction, the torpid form, was observed in two of the cases. In these cases the initial reaction subsided within three or four days, but lighted up again ten days and fifteen days respectively after inoculation and then went through the various stages of the typical luetin papule in one case and pustule in the other.

For purposes of analysis the cases to which the tests were applied may be divided into four series: Series "A" embodies cases exhibiting active secondary manifestations; Series "B" consists of cases showing tertiary lesions; Series "C" covers cases of syphilis with clear histories of infection, but, at the time, latent or cured; Series "D" embraces normal individuals, used as controls. A tabulation of these cases follows:

TABULATION OF LUETIN RESULTS.

SERIES A—SECONDARY SYPHILIS.

CASE 1.—Mucous patches in mouth and general adenopathy. Inunctions of mercury for five months early in 1911. Mercury internally for two months a year ago. Wassermann negative. Positive pustular luetin reaction.

CASE 2.—Mucous patch on tonsil and general adenopathy. Mercury and potassium iodide intermittently for four months in 1912. Wassermann negative. Positive pustular luetin reaction.

CASE 3.—Mucous patches in mouth. Treated with mercury for eleven months following infection. Wassermann positive. Luetin reaction positive papular ("Umstimmung").

CASE 4.—Mucous patches in mouth, and condylomata, general adenopathy, and osteocopic pains. Potassium iodide for three weeks followed by twelve injections of sodium cacodylate. Wassermann positive. Weak papular luetin reaction.

CASE 5.—Cachexia, alopecia, and osteoscopic pains. Salvarsan intravenously in May and November, 1912. Protoiodide by mouth during the past month. Wassermann positive. Luetin reaction negative.

CASE 6.—Mucous patches in mouth. Protoiodide by mouth for six months followed by two intravenous treatments with salvarsan and mercury by mouth during the last five weeks. Wassermann positive. Weak positive papular luetin reaction.

CASE 7.—Mucous patches under tongue. Inunctions of mercury for three weeks in May, 1912, followed by intramuscular injection

of salvarsan. Wassermann weakly positive. Positive pustular luetin reaction.

CASE 8.—Mucous patches and infiltration of fauces. Salvarsan intravenously in September, 1912. Wassermann weakly positive. Positive papular luetin reaction appearing on tenth day (torpid form).

CASE 9.—Mucous patches in throat. Salvarsan intravenously in March, 1912, followed inunctions of mercury for four weeks. Wassermann negative. Luetin reaction negative.

CASE 10.—Maculopapular eruption, adenopathy, and sore throat. Intravenous injection of salvarsan three days before tests were applied. Wassermann positive. Positive papular luetin reaction.

CASE 11.—Mucous patches in mouth and occasional osteocopic pains. Mercury by mouth and inunction for two months early in 1911. Salvarsan intravenously in June, 1911. Wassermann negative. Positive pustular luetin reaction.

CASE 12.—Mucous patches in mouth and general adenopathy. Salvarsan intravenously a month ago followed by four intramuscular injections of gray oil. Wassermann negative. Luetin reaction negative.

CASE 13.—General macular eruption, mucous patches, and adenopathy. Two intramuscular injections of gray oil followed by neosalvarsan intravenously forty-eight hours before tests were applied. Wassermann positive. Positive pustular reaction at site of luetin injection appearing fifteen days after inoculation. Papule at site of control ("Umstimmung").

SERIES B—TERTIARY SYPHILIS.

CASE 1.—Gummatous ulcers and cicatrices on leg. Primary sore seven years ago. Clear history of secondaries. Mercury and potassium iodide intermittently for past six years. Five injections of sodium cacodylate recently. Wassermann negative. Positive papular luetin reaction.

CASE 2.—Rupial lesions, alopecia, and general adenopathy. Chancre five years ago. Protoiodide and potassium iodide routinely during past two years. Seven injections of sodium cacodylate recently. Wassermann negative. Weak positive papular luetin reaction.

CASE 3.—Rupial lesions. Not certain of date of infection. Protoiodide by mouth during the past month. Twelve injections of sodium cacodylate. Wassermann negative. Weak positive papular luetin reaction.

CASE 4.—Persistent headache worse at night. Clear history of chancre in 1907, followed by secondaries. Intramuscular injections of mercury and potassium iodide by mouth from January

to April, 1908. "Cook's Remedy" during May, 1908. Mercury and potassium iodide during the entire year 1909. Wassermann negative seven consecutive times during the past seven months. Luetin reaction negative.

CASE 5.—Syphilitic orchitis. Denies infection or history of secondaries. Wassermann strongly positive before treatment—now negative. Salvarsan intravenously two weeks before application of tests followed by injection of gray oil. Wassermann negative. Positive pustular luetin reaction.

SERIES C—CONTROLLED SYPHILIS.

CASE 1.—Infected in September, 1911, clear history, no active lesions at present. Salvarsan intramuscularly in February, 1912, preceded and followed by inunctions of mercury. Wassermann strongly positive before treatment and negative at monthly intervals since that time. Positive papular luetin reaction.

CASE 2.—Infected in 1910, clear history, no active lesions at present. Mercury by mouth for two months following appearance of secondaries, salvarsan intramuscularly in 1911, and mixed treatment during the period August to October, 1912. Wassermann negative. Positive papular luetin reaction.

CASE 3.—Infected in 1894. No active lesions at present. Has been treated intermittently with mercury during past eighteen years. Wassermann negative. Strong positive pustular luetin reaction.

CASE 4.—Infected in May, 1911. No symptoms at present. No definite history of treatment can be procured. Wassermann negative. Positive papular luetin reaction.

CASE 5.—Infected a year ago. No active lesions. Mercury by mouth for nine months following infection. Wassermann weakly positive. Positive pustular luetin reaction.

CASE 6.—Infected in October, 1911. No symptoms at present. Protoiodide for nine months followed by potassium iodide for past three months. Wassermann negative. Positive pustular luetin reaction.

CASE 7.—Infected a year ago. No lesions at present. Treated with protoiodide for three months followed by twelve injections of sodium cacodylate. Wassermann strongly positive. Weak positive papular luetin reaction.

CASE 8.—Infected in June, 1909. No lesions at present. Received inunctions of mercury for one month in 1909 followed by a specific mixture (nature not elicited) for a year. No treatment during 1911–12. Wassermann negative. Weak positive papular luetin reaction.

CASE 9.—Infected in 1907. No active lesions at present. Mercury by mouth and inunction for one year. No treatment during

past four years. Wassermann weakly positive. Weak positive papule at both luetin and control sites ("Umstimmung").

CASE 10.—Infected in 1911. No symptoms at present. Wassermann strongly positive before treatment. Salvarsan intravenously in May, 1911. Wassermann negative. Positive pustular luetin reaction.

CASE 11.—Infected in 1904. No active lesions at present. Mercury during the entire year 1905 and potassium iodide during June, 1912. Wassermann positive in April, 1912, now negative. Distinct positive papular luetin reaction.

CASE 12.—Infected in 1902. No active lesions now. Wassermann positive on five occasions during the period April to October, 1911. Two intravenous and one intramuscular administrations of salvarsan in March, June, and October, 1911, respectively. Wassermann now weakly positive. Luetin reaction negative.

CASE 13.—Infected in June, 1912. No lesions at present. Wassermann positive before treatment. Salvarsan intravenously on November 4 and 23, 1912, followed by four injections of gray oil. Wassermann reaction still positive. Luetin reaction negative.

CASE 14.—Infected in October, 1911. No symptoms at present. Wassermann positive before treatment. Inunctions of mercury during November, 1911. Protoiodide by mouth during February, 1912, followed by salvarsan. Wassermann negative. Positive papular luetin reaction.

CASE 15.—Infected in December, 1911. No lesions at present. Wassermann weakly positive before treatment. Intramuscular injection of salvarsan, January 28, 1912. Wassermann negative. Weak positive papular luetin reaction.

CASE 16.—Infected in July, 1912. No manifestations at present. Inunctions of mercury during the past six months. Wassermann weakly positive. Weak papular luetin reaction.

CASE 17.—Infected in October, 1910. No active lesions at present. Wassermann reaction strongly positive on several (five) occasions before and after treatment. Mercury during March, 1911, followed by intravenous treatment with salvarsan. Salvarsan intramuscularly on September 7, 1911. Wassermann now negative. Distinct papular reaction at sites of injection of both luetin and control ("Umstimmung").

CASE 18.—Infected in May, 1909. No active manifestations. Mercury for one month in 1909. Patient denies further treatment. Wassermann negative. Weak positive papular luetin reaction. (Constitutional manifestations followed the injection of luetin in this case. Patient complained of "soreness all over," and browache forty-eight hours after inoculation. Temperature, 102° F. All symptoms disappeared, without treatment, in twenty-four hours.)

CASE 19.—Infected in August, 1911. Salvarsan intravenously in September, 1911, December, 1911, and April, 1912. Wassermann negative. Positive pustular luetin reaction (state of "Umstimmung" present for five days).

CASE 20.—Infected for eighteen months. No active lesions. Mercury by mouth for one month during 1912. Wassermann negative. Positive papular luetin reaction ("Umstimmung").

CASE 21.—Infected August 25, 1911. No symptoms at present. Wassermann positive before treatment. Inunctions of mercury for three weeks in September, 1911; salvarsan intravenously in October, 1911; intramuscular injections of mercury in October, 1911. Wassermann negative. Positive pustular luetin reaction.

CASE 22.—Infected in January, 1902. No active manifestations. Wassermann positive before treatment. Mercury for two years, 1901–02. Salvarsan intravenously September 19, 1911. Wassermann negative. Positive papular luetin reaction.

CASE 23.—Infected in July, 1911. No active lesions at present. Mercury for three months in 1911. Wassermann negative. Positive papular luetin reaction.

CASE 24.—Infected in December, 1909. No active lesions now. Wassermann positive early in 1911. Salvarsan intravenously in March, and again in April, 1911. Wassermann negative. Positive papular luetin reaction.

CASE 25.—Infected in September, 1911. No manifestations at present. Wassermann strongly positive before treatment. Salvarsan intramuscularly November 27, 1911. Wassermann weakly positive. Positive pustular luetin reaction.

CASE 26.—Infected in February, 1909. Clear history of typical secondaries. Wassermann positive on five occasions during the period July to October, 1911. Salvarsan intravenously in July, 1911. Wassermann negative. Weak positive papular luetin reaction.

CASE 27.—Infected in 1909. No active lesions at present. Protoiodide by mouth for eighteen months during 1910–11. Wassermann strongly positive. Positive pustular luetin reaction.

CASE 28.—Infected in December, 1911. No active manifestations now. Wassermann negative at monthly intervals for six months following treatment, though positive prior to treatment. Salvarsan intramuscularly February 3, 1912. Patient gained twenty-five pounds after treatment. Wassermann still negative. Luetin reaction negative.

CASE 29.—Infected in December, 1911. No active lesions since treatment. Positive Wassermann before treatment. Salvarsan intramuscularly February 3, 1912. Wassermann negative. Positive papular luetin reaction.

CASE 30.—Infected in February, 1912. No active lesions at present. Wassermann positive before treatment and persisted after first treatment with salvarsan. Salvarsan intravenously in

May and August, 1912. Wassermann negative after second treatment but now positive. Weak positive papular luetin reaction.

CASE 31.—Infected in 1902. No manifestations at present. Four consecutive positive Wassermann tests in the period October, 1911, to February, 1912. Salvarsan intravenously in September, 1911. Wassermann negative. Weak positive papular luetin reaction.

CASE 32.—Infected in November, 1911. No symptoms at present. Wassermann positive before treatment. Salvarsan intravenously February 3, 1912. Wassermann negative. Positive pustular luetin reaction.

CASE 33.—Infected in November, 1911. No lesions now. Inunctions of mercury followed by salvarsan intravenously in March, 1912. Wassermann positive before treatment with salvarsan, now negative. Weak positive papular luetin reaction.

CASE 34.—Infected in October, 1911. No active lesions at present. Wassermann positive in June, 1912. No record of treatment and soldier denies having been treated elsewhere. Wassermann now negative. Positive pustular luetin reaction. (Distinct pustule appeared at site of control injection sixteen days after inoculation. Its development was coincident with the beginning disappearance of the luetin pustule. Delayed "Umstimmung?")

CASE 35.—Infected in 1901. No active manifestations at present. Wassermann strongly positive in April, 1911. Salvarsan intravenously April 18, 1911. Wassermann subsequently and now negative. Weak positive papular luetin reaction.

CASE 36.—Infected in February, 1911. No symptoms at present. Two intravenous and one intramuscular administrations of salvarsan during April and May, 1911. Mercury and potassium iodide during July, 1912. Wassermann negative. Positive papular luetin reaction.

CASE 37.—Infected in July, 1912. Clear history and positive Wassermann before treatment. Inunctions of mercury for one week followed by salvarsan intravenously on September 18, 1912. Wassermann negative. Positive papular luetin reaction.

CASE 38.—Infected in December, 1910. No manifestations at present. Protoiodide by mouth for three months followed by salvarsan intramuscularly. Wassermann weakly positive. Positive papular luetin reaction.

CASE 39.—Infected in 1905. No active lesions. Wassermann positive a year ago. Inunctions of mercury for two months followed by salvarsan intramuscularly on May 22, 1912. Wassermann negative. Weak positive papular luetin reaction.

CASE 40.—Infected in July, 1912. Typical secondaries in September. No lesions at present. Salvarsan intravenously three times during the past three months. Wassermann negative. Positive papular luetin reaction.

CASE 41.—Infected October 4, 1911. Wassermann positive November 5, 1911. Inunctions of mercury from November 3, 1911 to January 26, 1912. Salvarsan intramuscularly November 12, 1911. No lesions at present. Wassermann negative. Positive papular luetin reaction.

CASE 42.—Infected in July, 1909. Wassermann positive in July and November, 1911. Salvarsan intravenously July 2, 1911, followed by inunctions for three months and mercury by mouth for one month. No active manifestations now. Wassermann negative. Weak positive papular luetin reaction.

CASE 43.—Infected in February, 1910. Wassermann strongly positive in June, 1911. Intramuscular injections of mercury May to October, 1910. Salvarsan intravenously June 26, 1911. No lesions now. Wassermann negative. Positive papular luetin reaction.

CASE 44.—Infected in April, 1912. Wassermann weakly positive in May, 1912. Salvarsan intravenously May 23, 1912. No symptoms during past six months. Wassermann negative. Luetin reaction negative.

CASE 45.—Infected in March, 1908. Clear history of secondaries. Treated with mercury from June, 1909, to May, 1910, potassium iodide during July, 1910, salvarsan intravenously March 29, 1911. Wassermann negative. Positive pustular luetin reaction.

CASE 46.—Infected in 1907. Wassermann positive in October, 1912. Treated energetically with mercury for two years, 1907–09. Salvarsan intravenously in October, 1912. Wassermann test has been negative at monthly intervals since treatment with salvarsan. Patient is somewhat anemic, but exhibits no active manifestations. Weak positive papular luetin reaction.

CASE 47.—Infected in 1898. Clear history of secondaries. Wassermann reaction positive before and after treatment in 1911, at Manila, P. I. Salvarsan intravenously, at Manila, P. I., in July, 1911. Wassermann negative at monthly intervals for past four months. No active lesions at present, but patient is anemic and below normal tone. Positive papular luetin reaction.

CASE 48.—Infected in October, 1911. Disease ran a malignant course and was not influenced by mercury. Wassermann strongly positive before treatment with salvarsan. Salvarsan intravenously in March, 1912, followed by inunctions of mercury for three months, and mixed treatment during July, 1912. No active lesions now. Wassermann negative. Strong positive papular luetin reaction.

CASE 49.—Infected in October, 1911. Wassermann positive in November, 1911. Chancre excised, salvarsan administered intramuscularly, followed by inunctions of mercury for two months. Patient gained weight, has remained without symptoms, and Wassermann has been negative at monthly intervals to date. Luetin reaction negative.

CASE 50.—Infected in December, 1911. Wassermann positive January 15, 1912. Salvarsan intravenously January 16 and 24, 1912. No active lesions during 1912. Wassermann negative. Positive papular luetin reaction.

CASE 51.—Infected in June, 1911. Typical secondaries—mucous patches, maculopapular eruption, alopecia, and adenopathy. Wassermann tests at Fort Leavenworth and Washington laboratories repeatedly negative before treatment. Salvarsan intravenously November 4 and November 27, 1912, followed by two injections of gray oil. No active lesions at present. Wassermann negative. Weak positive papular luetin reaction ("Umstimmung").

CASE 52.—Infected in June, 1910. Wassermann positive in July, 1911. Salvarsan intravenously in July, 1911, followed by mixed treatment for one month. Protoiodide by mouth during December, 1911. No active manifestations since that time. Wassermann negative. Luetin reaction negative.

SERIES D—CONTROL CASES.

CASE 1.—Married, non-commissioned officer with healthy children. Denies venereal history. Diphtheria a year ago. Throat culture positive for K–L bacillus. Wassermann at that time negative. No antisyphilitic treatment. Wassermann negative. Luetin test negative.

CASE 2.—Robust young soldier. Denies venereal disease. Careful physical examination fails to reveal signs of acquired syphilis or any of the stigmas of congenital lues. These findings concurred in by one of the best syphilographers in the army. Wassermann negative. Typical strong positive papular luetin reaction. Family history shows one grandparent to have had tabes.

CASE 3.—Normal young adult male (laboratory assistant). No history of venereal disease. Wassermann and luetin tests negative.

CASE 4.—Young soldier. Denies venereal disease. No clinical evidence of congenital or acquired lues. Wassermann negative. Luetin test negative.

CASE 5.—Young soldier. Has three typical chancroids which appeared five days after intercourse. History of a single sore, similar to those he now exhibits, three years ago. Treated locally by a druggist and healed in a week or so. No specific treatment. No clinical evidences of syphilis. Wassermann negative. Luetin test negative.

ANALYSIS OF RESULTS. By reference to the above summary it will be observed that the luetin test was applied to 13 cases of secondary treated syphilis; 5 cases which exhibited tertiary lesions;

52 cases of syphilis in the stage of latency or cure; and 5 individuals presumably free from syphilis.

The percentage of positive reactions among the treated cases of secondary lues was 77 per cent.; of the tertiary cases, 80 per cent. reacted positively; while among the cases which had reached a stage of latency, 88 per cent. gave a positive reaction. Of the 5 apparently normal individuals used as controls, 1 case developed a typical papular reaction. This occurrence is of considerable moment, as the value of the test hinges largely on its specificity. The case in question was that of a perfectly healthy young soldier who denied absolutely the possibility of syphilis. Careful physical examination failed to demonstrate signs of syphilis, and the Wassermann test was negative on three occasions. The family history revealed the fact that the maternal grandmother suffered with an ailment for several years which, from the recital of symptoms, was probably tabes. It has been demonstrated experimentally that the state of allergy or anaphylaxis (upon which the luetin reaction depends) may be transmitted from a sensitized guinea-pig to her offspring and that this transmission can occur only through the female. This raises the very interesting query as to whether a state of allergy, transmitted from a luetic maternal grandmother, might not explain the positive luetin reaction in the case under discussion. Personally, I am inclined to this belief, for, in view of the mass of evidence in favor of the specificity of the test as the result of observations of numerous investigators covering hundreds of cases, it would be presumptious to contend that the test is not specific because of this one apparently discordant result.

The relative value of the Wassermann and luetin tests is strikingly illustrated in the above series of cases. An opportunity was not offered to apply the luetin test to cases of primary or secondary untreated syphilis, but the work of others seems to show definitely that the reaction rarely occurs in the early stages of the disease. It is in the earlier stages of syphilis that the highest percentage of positive results are obtained with the Wassermann test, while in the later stages the lipotropic substances, upon which a positive reaction depends, are frequently not present in the serum due to fluctuations in the activity of the spirochetæ, induced by treatment or by the production of antibodies which neutralize these lipotropic substances. On the other hand, these fluctuations in the activity of the spirochetæ favor the development of the state of allergy or anaphylaxis, which must be induced before the skin will react to the injection of luetin. In other words, a positive Wassermann test indicates the presence of metabolic substances in the serum, due to present or recent activity of numbers of spirochetæ on the tissues; while a positive luetin reaction is indicative of a state of hypersensitiveness to the specific

proteins of the spirochetæ, induced by a period of cessation of the introduction of these proteins prior to the injection of the luetin.

The results obtained practically with the Wassermann and luetin tests in my series of cases supports the foregoing theoretical assumption. The cases which reacted most intensely to the luetin were, as a rule, those in which the Wassermann test was negative, and *vice versa*.

A casual glance at the brief summaries of the cases outlined above will show the value of the luetin test as a diagnostic measure in the tertiary and latent stages of syphilis, but its greatest value, from my limited experience, appears to be as a means of prognosis. In seventy cases of undoubted syphilis, practically all of whom had been treated, either clinical evidence, a positive Wassermann test, or a positive luetin reaction showed that the syphilitic infection had not been entirely suppressed in all but four cases. It seems reasonable to assume that these latter cases (Cases 28, 44, 49, and 52, Series "C") may be registered as cured.

In view of these results, a provocative injection of salvarsan followed by the application of both Wassermann and luetin tests is suggested as a rational means of determining whether treatment has been sufficiently intensive to effect a cure.

It is a pleasure to thank Dr. Hideyo Noguchi, of the Rockefeller Institute, New York City, for the luetin used in the tests reported herein, and to acknowledge my indebtedness to Major F. M. Hartsock, Medical Corps, United States Army, and Dr. Yohe, of the Federal Penitentiary, Leavenworth, Kansas, for the cases to whom the tests were applied.

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DORSAL PERCUSSION IN ENLARGEMENTS OF THE TRACHEOBRONCHIAL GLANDS.

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This study represents an attempt to determine the practical diagnostic value of vertebral percussion in that familiar group of tracheobronchial enlargements so frequently met with as sequels of pertussis, measles, and tonsillitis, and as the result of tuberculosis. Secondarily, data has been sought whereby differences might be established between the percussion findings in simple adenopathies and in the more extensive neoplastic tumors of the mediastinal space. As a basis of comparison, in the cases under consideration the normal acoustic and tactile characteristics of the percussion zones of the spine were taken as criteria, together with certain acknowledged modifications thereof produced by different thoracic diseases: fibroma, malignant tumor, gumma, and dense fibrosis of the lungs and pleura. Lesions such as these account for physical signs relating not only to the thoracic walls, but also to the thoracic segment of the spine, where more or less definite tonal and topographic changes in the normal percussion zone are apparent.

The dulling effect of tracheobronchial adenopathies upon the thoracic wall has long been an accepted fact, but comparatively few clinicians have championed the procedure of vertebral percussion as a means of investigating this very common and often overlooked condition. One-fourth of all cases of healed pulmonary tuberculosis reveal tracheobronchial adenopathies at autopsy, according to Adami and McCrae.[1] As long as fifteen years ago Fernet[2] drew attention to the causal relationship between tuberculous bronchial adenitis and bilateral paraspinal dulness, but the dulling of the spine itself under a similar circumstance was not fully appreciated as a clinical finding until the appearance of von Korányi's convincing studies of vertebral percussion, eight years later.[3] This despite Ewart's important article on "Dorsal Percussion," published in 1899.[4] This author, employing instrumental pleximeter percussion, delineated upon the normal spine an isolated relative dulness of the fifth thoracic spine attributable to the "influences due especially to the infratracheal glands," and he also mapped out areas of "visceral dulness" over segments of the spine corresponding to the heart and the liver. As an illustration of the relative frequency of spinal and of mural dulness in tracheo-

[1] Trans. Sixth Internat. Congress for Tuberculosis, 1908, i, 325.
[2] Bull. de l'Acad. de méd., 1898, xl, 253.
[3] Zeitschr. f. klin. Med., 1906, lx, 295.
[4] Lancet, 1899, ii, 261.

bronchial enlargements it is instructive to note the results obtained by Stoll,[5] who found the incidence virtually the same (22 per cent. and 23 per cent. respectively) in 175 patients, presumably subjects of bronchoadenopathy. For more recent studies on the diagnosis of this condition and the application of dorsal percussion thereto the reader is referred to articles by Philippi and Schultz,[6] by Grenet,[7] and by Zabel.[8]

Honeij's clinical examinations[9] of 147 patients with questionable and proved phthisis showed that approximately 24 per cent. had enlarged glands at the root of the lung, while still more noteworthy is the same author's uniform demonstration of mediastinal adenopathy in a series of 32 non-tuberculous subjects, classified as "questionable" and as "proved negative" with regard to the diagnosis of pulmonary tuberculosis.

In the healthy adult, gentle finger percussion of the thoracic vertebral processes yields an upper zone of impaired resonance, with appreciable tactile resistance over the first two or three spines, below which there is uniform osteal resonance over the remaining spinous tips. This upper hyporesonant zone has been carefully studied and delineated by Korányi,[10] and although this author's conclusions have not received merited recognition in all quarters, his findings should be obvious to anyone who, careful of technique, studies the subject with an open mind. The relative dulness of the upper thoracic vertebræ is best explained by assuming that these osseous disks are more or less sensitive to the dulling properties of the adjacent cervical segment of the spine. The cervical spine, despite its intimate proximity to the prevertebral air passages and to the esophagus, is anatomically unfitted to generate wholly resonant percussion waves, for such attempts are damped, at least to some degree, by the unyielding, rigid structure of this part of the spine due to its short length, compact components, tense ligamentous attachments, and absence of articulating ribs for the conduction of lateral vibrations. These and the other peculiarities of the thoracic spine in its role as a pleximeter in the production and transmission of percussion waves have been discussed in detail by the writer in an earlier article.[11]

Ewart[12] calls attention to the clinical utility of mapping out, by pleximetric percussion, an ovoid parasternal area of impaired pulmonary resonance between the levels of the first and the fifth thoracic vertebral spines. This area, termed the "sub-

[5] Cited by Honeij, v. i.
[6] Beitr. z. klin. d. Tuberkulose, 1911, xxi, 116.
[7] Ann. de méd. et chir. infant., 1911, xv, 497.
[8] Münch. med. Woch., 1912, lix, 2664.
[9] Jour. Amer. Med. Assoc., 1911, lvii, 958.
[10] Loc. cit.
[11] Amer. Jour. Med. Sci., 1909, cxxxviii, 815.
[12] British Med. Jour., 1912, ii, 966.

resonant interspinous dull patch," in the normal adult extends vertically for a distance of about 110 mm., and has a transverse equatorial diameter of approximately 90 mm., each lateral boundary being equidistant from the midspinal line. Ewart, furthermore, is able to distinguish a normal respiratory variation in the transverse extent of this area, which contracts laterally with deep inspiration and correspondingly expands with expiration, as the volume of the adjacent lungs alternately increases and diminishes. The real value of the "subresonant patch" in the study of tracheobronchial glandular tumors (which lesions can be reasonably expected to alter the characteristic ovoid outline and to restrict the respiratory contour) is still undetermined in the absence of convincing clinical data. Personally, attempts to employ Ewart's area in investigating mediastinal lesions proved of no more conclusive value than the more familiar manner of percussing the dorsal thorax according to conventional technique.

Apropos of the subject of dorsal percussion in general, it may be remarked that a similar technical difficulty would seem to bar the general application of Minerbi's clever, though most delicate, procedure[13] of delimiting a so-called "aortic and azygos vein zone of dorsal hyporesonance:" a paravertebral area of impaired resonance about 34 cm. long, at the level of the third thoracic spine, and corresponding anatomically to the impingement of the aorta and of the azygos vein upon the mediastinal wall.

Intrathoracic Factors of Vertebral Percussion Sounds. The exact mechanism whereby intrathoracic lesions, particularly those springing from the mediastinal space, affect the percussion sounds over the cervical vertebræ is determined chiefly by the intrinsic conditions prevailing in the individual case; but it also depends to some extent upon various extrinsic forces whose action, exceptionally, is even more potent than that of the underlying gross pathological condition. These extrinsic forces, in order not to cloud the more important argument under consideration, may be dismissed by admitting, on *a priori* grounds, the hyporesonating influence of a generous dorsal musculature and adipose covering; of excessive ligamentous tension; of undue depth of the spinal groove; of spinal deformity and other diseases of the vertebral column interfering with its vibratory action under the impact of the percussion blow. Omitting, then, from further consideration these secondary influences, a number of intrinsic conditions remain to be interrogated.

The intrinsic clinical group includes lesions of the mediastinum, the lungs, and the pleura, in this order of importance, as accounting for vertebral physical signs. Mediastinal lesions, in the form of tracheobronchial adenopathies, with which this

[13] Semaine méd., 1912, xxxii, 342.

paper deals in particular, are by far the most frequent as well as the most important of the three intrathoracic conditions mentioned, and court special attention because of the apparently paradoxical findings with which not infrequently they have a direct casual relationship. This is notably true in certain cases that otherwise afford consistent clinical data, whether relating to the history, to the mural signs, or to the radiograph. Thus, on the one hand, in one patient with urgent dyspnea, distinct cyanosis, and a radiographic picture of enlarged bronchial glands the thoracic spines may yield a sonorous hyperresonance, while, on the other hand, this region may be frankly dull and non-resilient in another patient just as characteristically hall-marked as the first one. Making due allowance for the extrinsic modifying factors noted above, the explanation of such a contradictory state of affairs should be sought by an inquiry into the anatomic peculiarities of the glandular mass and by an attempt to determine its conducting properties of the vocal and the percussion vibrations.

TONAL CONDUCTION *vs.* COMPRESSION DULNESS. With reference to its anatomic peculiarities, the size, the shape, and the situation of a given mediastinal mass are the main points to be investigated in connection with the physical signs. In brief, to afford any tangible signs whatever the mass must be of such a nature that it either (1) encroaches backward upon the vertebral column, or (2) acts as an intervening conducting medium—two pathologic conditions that determine diametrically opposite objective symptoms.

1. In the first instance the close impingement of a foreign body of considerable size against the mediastinal surface of the spine may effectually damp the normal vibrations thereof, and, in addition to this primary subresonating influence, may lend to the vertebral percussion sound a certain measure of its own dulness. Under such a circumstance frank dulness combined with undue tactile resistance is to be expected when the thoracic spinous tips are percussed, the conspicuousness of this external retrovertebral change being roughly commensurate with the extent of its internal antevertebral factor.

This explanation, it will be noted, presupposes the existence of a mediastinal mass close against the spine, but acoustically remote from the great air passages, and consequently in nowise concerned in the transmission of intratracheal and intrabronchial tones excited by phonation or by percussion. In the case of tracheobronchial adenopathies this condition of glandular encroachment without adequate conducting properties is, in the writer's experience, more frequent than the transmission of paraglandular tones, next to be mentioned. It must be added, however, that unlike other tumors of the mediastinal space simple glandular enlargements do not, as a rule, reach sufficient bulk extensively to

modify either the spinal or the mural vibrations of the thorax posteriorly.

2. In the second instance, that of an intervening conductor of the tracheobronchial tone, it is essential (*a*) that the glandular mass be situated so as to act as an efficient transmission path for sounds originating within the large air passages; and that (*b*) the resonance of these transmitted sounds must predominate at the thoracic segment of the spine to such a degree as to stifle any inherent dulness that the foreign body otherwise might exhibit. Here, therefore, it is to be assumed that the mass, even though it be of large size and closely abutting the mediastinal spine, also is intimately related to the trachea (or even to the gullet), so that the vibrations therein set up travel to the spine through this adenoid path, and, being comparatively the louder and the more sonorous, efface every trace of dulness. By a similar mechanism mediastinal neoplasms may hyperresonate the thoracic spine to an extreme degree —usually to a much greater extent than do simple adenoid growths —and in this connection Stradiotti's work[14] on vertebral percussion in compression of the trachea by tumors of the anterior mediastinum, is of great practical interest.

The conducting properties of a mediastinal mass must be taken into account, especially when dealing with a growth firmly wedged between the air passages and the spinal column, inasmuch as such a lesion, no matter how perfectly it conforms mechanically to the essentials of a propagation tract for sound waves, cannot so act unless its histologic structure is adapted to this purpose. Other conditions being the same, a dense, compact structure under moderate tension proves a better conductor than one composed of boggy, relaxed tissue. A mediastinal fibroma is more likely to transmit tracheal hyperresonance backward than to betray its presence by merely dulling the vertebræ; on the contrary, a vascular sarcoma commonly impairs rather than exaggerates the osteal percussion resonance. Of the truth of these clinical facts, academic though they may appear, the writer has been repeatedly convinced by cases observed from bedside to autopsy. Enlarged tracheobronchial glands, although structurally ideal as sound conductors, only exceptionally form the necessary acoustic bridge from air passage to spine, and by fault of this omission must more often dull than resonate this bone. This, however, does not seem to be true of their conduction of the spoken voice, according to d'Espine's experience, which argues a clearer transmission of vocal than of percussion vibrations along a glandular route of this sort. This writer has described[15] the association of pectoriloquy and striking hyperresonance over the upper thoracic vertebræ as a common finding in cases of enlarged peribronchial and peritracheal

[14] Policlinico, 1911, xviii, 285.

[15] Bull. de l'Acad. de méd., Paris, 1907, lvii, 167.

glands. Koch[16] has found the same change in esophageal carcinoma, the inference being that the tracheal sounds were conveyed spineward by dense intervening cancerous tissue. From the study of this series of tracheobronchial cases, the constancy of d'Espine's tympany-pectoriloquy sign cannot be confirmed, although its frequent demonstration is possible, insofar as the detection of clear pectoriloquy is concerned.

Summary of Results. The 18 case histories taken as the basis of this report were selected from a series of 38 mediastinal cases which afforded definite vertebral percussion findings. They represent, it is believed, typical examples of these signs, depending wholly upon the adenopathies in question and not upon the limited pleuropulmonary lesions coexisting in a few instances. No case of enlarged bronchial glands associated with some other large mediastinal mass (*i. e.*, carcinoma, fibroma, gumma) has been included in the summary, in order to rule out, so far as possible, extensive neoplastic tumors as potential factors of the spinal changes noted. Aside from the clinical histories the diagnoses were determined by the ordinary mural signs and by radiographs, most of which were the work of Dr. W. F. Manges, of the Jefferson Hospital.

The individual vertebral physical signs of the 18 tracheobronchial cases may be summarized and charted according to the following groups: (1) Interscapular dulness, above the level of the inferior scapular angles, or over the first seven thoracic spinous processes. (2) Infrascapular dulness, below the level of the inferior scapular angles, or over one or more of the five lower spinous tips. (3) General thoracic hyperresonance over the entire thoracic segment. (4) Normal percussion signs over the entire thoracic segment.

1. *Interscapular Dulness.* (Figs. 1 to 5.) To this group belong two-thirds of the series, or 12 cases, 6 affording uniform dulness to the fifth thoracic vertebræ (Cases I, III, XII, XIV, XVI, XVIII); 3, uniform dulness to the sixth (Cases VII, X, XI); and 1, dulness over the fourth, fifth, and sixth vertebræ (Case XIII). Of the 2 remaining cases of this group, 1 showed uniform dulness from the first to the seventh tips (Case VI), and the other a small basal dull patch over the sixth and the seventh vertebræ (Case XV).

In the group of six cases affording uniform dulness over the first five thoracic vertebræ (Fig. 1) but a single one (Case XIV) showed evidences of pleuropulmonary disease in addition to the mediastinal adenopathy. In this patient there was no reason to attribute the vertebral dulling to the coexisting lesion—chronic phthisis and left pleural adhesions of moderate development. Here the *x*-ray revealed a huge mass of enlarged glands at the tracheal bifurcation, and also many small nodules distributed through

[16] Tribune méd., 1912, viii, 381.

both lungs, but without cavity, disseminated fibrosis, or large consolidation. The same comment is applicable to Case XVI, one of tuberculous adenitis of the cervical, supraclavicular, and

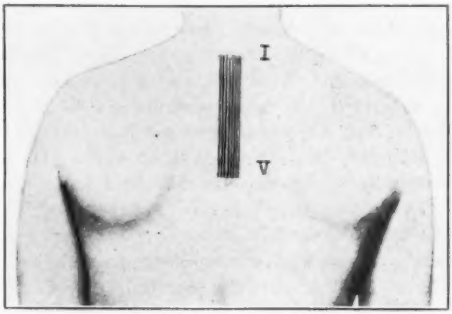

FIG. 1.—Interscapular dulness. Group of six cases, with uniform dulness and increased tactile resistance from the first to the fifth thoracic vertebra.

CASE I.—Unproductive cough; dyspnea on exertion; substernal pain and oppression for fourteen days, following a pneumonic crisis.

CASE III.—Unproductive paroxysmal cough; attacks of dyspnea; substernal pain and oppression; hoarseness. Symptoms of two years' duration, associated with numerous recurrent attacks of tonsillitis, and with a history of measles and pertussis in infancy.

CASE XII.—Unproductive cough; dyspnea; jugular fulness; facial tumefaction and venous tortuosity; substernal and interscapular pain.

CASE XIV.—Cough, with mucopurulent sputum; dyspnea on exertion; pleural pain; left-sided chronic adhesive pleurisy; chronic pulmonary tuberculosis.

CASE XVI.—Habitual dyspnea; cyanosis, venous congestion, and tumefaction of face, neck arms, and upper thoracic wall; laryngeal voice; paroxysmal aphonia and hoarseness; dysphagia. Bilateral cervical, supraclavicular, and axillary adenitis.

CASE XVIII.—Unproductive cought; habiual dyspnea; substernal oppression; dysphagia; recurrent bronchorrhea; jugular distention; venous tortuousity of neck and upper thoracic wall.

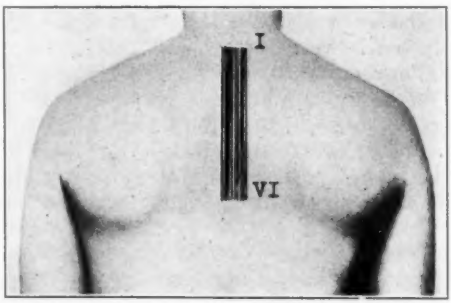

FIG. 2.—Interscapular dulness. Group of three cases, with uniform dulness and increased tactile resistance from the first to the sixth thoracic vertebra.

CASE VII.—Cough; orthopnea; cyanosis; vertigo; pleural pain.

CASE X.—Unproductive cough; dyspnea; vertigo; syncope; substernal pain; enlargement and tortuousity of superficial venules of upper thoracic wall. Chronic adhesive pleurisy.

CASE XI.—Dyspnea; cough with mucopurulent sputum; pleural pain; restricted respiratory excursion; chronic bilateral adhesive pleurisy; bilateral cervical and axillary adenitis.

axillary nodes, and with apparently normal lungs and pleuræ. The foregoing cases, then, seem fairly to represent the dulling effect of uncomplicated tracheobronchial enlargements upon the upper thoracic segment. In none of the other cases of this group was the glandular mass excessive, though in all it was an obvious finding.

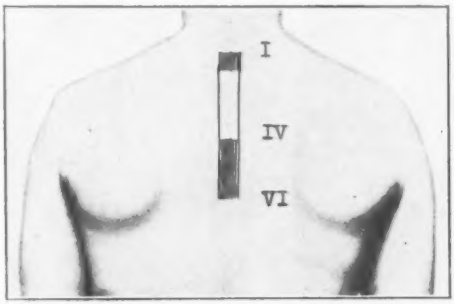

FIG. 3.—Interscapular dulness. Dulness and increased tactile resistance over the first, fourth, fifth, and sixth thoracic vertebræ; hyperresonance over the second and third.
CASE XIII.—Unproductive cough; moderate dyspnea and substernal oppression. Chronic fibroid pulmonary tuberculosis.

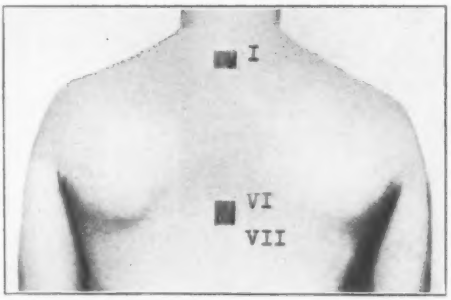

FIG. 4.—Interscapular dulness. Dulness over the first, sixth, and seventh thoracic vertebræ.
CASE XV.—Unproductive cough; habitual dyspnea; recurrent bronchitis; pleural pain. Chronic pulmonary tuberculosis, with extensive compensatory dilatation of both lungs.

Of the 3 examples of uniform dulling of the first six thoracic spinous processes (Fig. 2), 2 had generalized pleural thickening, and in 1 of these patients the cervical and the axillary glands were moderately enlarged. In all 3 the lungs were unaffected. As may be noted by the case notes summarized under Fig. 2, urgent pressure symptoms and pleural complications were conspicuous in this group, in none of which, however, did the radiograph show an extraordinary enlargement of the mediastinal lymph nodes. There is no convincing reason to account for a

lower level of thoracic dulness in these cases than in the preceding six, for the adenopathies were, if anything, of more moderate size. So in the absence of positive proof, one can but suggest as potential factors disproportionate backward growth of the affected glands, and, possibly, damping of the spinal vibrations by excessive pleural thickening and contraction.

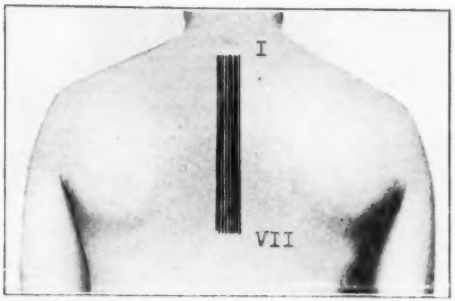

FIG. 5.—Interscapular dulness. Uniform dulness and increased resistance from the first to the seventh thoracic vertebra.

CASE VI.—Cough; dyspnea; cyanosis; substernal oppression; venous congestion and edema of the anterior thoracic wall.

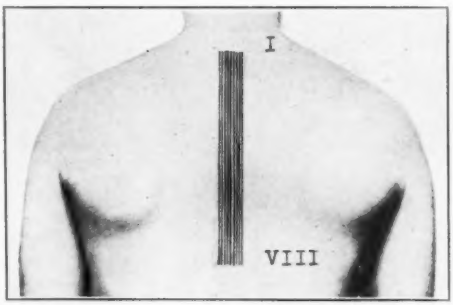

FIG. 6.—Infrascapular dulness. Uniform dulness and increased tactile resistance from the first to the eighth thoracic vertebra.

CASE VIII.—Extensive chronic adhesive pleurisy, with moderate pain, unproductive cough, and dyspnea.

In Case XIII (Fig. 3), with a patch of hyperresonance over the second and the third vertebræ, extensive compensatory dilatation of the posterior pulmonary margins was the predominant clinical feature. Case XV (Fig. 4) showed an even longer zone of spinal hyperresonance, and here also the lungs were greatly overdistended posteriorly. From these facts the association of the pulmonary and the osteal hyperresonance in casual relationship is the natural inference. In Case VI (Fig. 5) a large tracheobronchial tumor

with distressing pressure symptoms, but with normal lungs and pleuræ, was found, in combination with unbroken dulness over the upper seven vertebræ. Apparently this illustrates dulling by glandular pressure minus the modifying effects of concomitant pulmonary emphysema, pulmonary fibrosis, or pleural thickening.

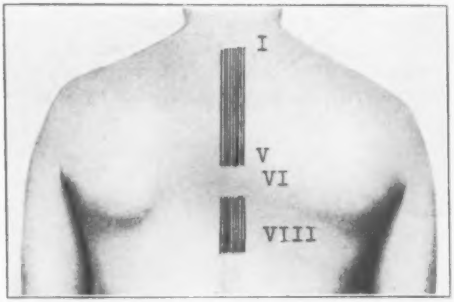

FIG. 7.—Infrascapular dulness. Dulness and increased tactile resistance from the first to the fifth thoracic vertebra, with impaired resonance over the seventh and eighth.

CASE XVII.—Unproductive cough; pleural pain; dyspnea on exertion; substernal oppression. Chronic bilateral pulmonary tuberculosis and adhesive pleurisy.

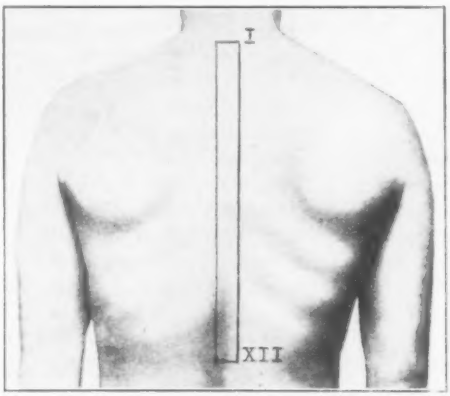

FIG. 8.—General thoracic hyperresonance. Group of three cases, with uniform hyperresonance and tactile resiliency from the first to the twelfth thoracic vertebra.

CASE II.—Unproductive cough; paroxysms of vomiting; striking dyspnea; substernal oppression for sixteen days, following a severe attack of bronchopneumonia, chiefly of the right upper pulmonary lobe.

CASE IV.—Irritative cough, occasionally attended with dark mucoid sputum; substernal pain and oppression; moderate habitual cyanosis; interscapular pain and aching.

CASE V.—Unproductive cough; dyspnea on slightest exertion; vomiting provoked by coughing; substernal pain and oppression; chronic follicular tonsillitis. Symptoms of four years' duration, and first observed a few months after recovery from diphtheria.

2. *Infrascapular Dulness* (Figs. 6 and 7). In the two instances of dulness below the level of the inferior scapular angles the zone

of hyporesonance over the first eight thoracic vertebræ was uniform in one case (Case VIII) and interrupted by a resonant sixth vertebral tip in the other (Case XVII). In both patients the glandular enlargement was accompanied by extensive pleural adhesions, and in one by bilateral pulmonary tuberculosis, neither of which conditions seemed satisfactorily to account for the spinal signs.

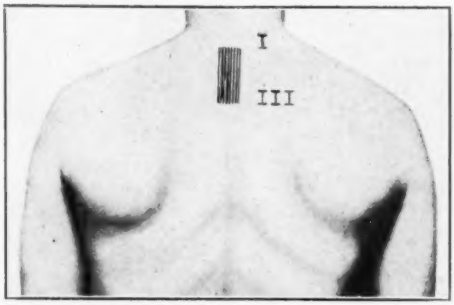

FIG. 9.—Normal thoracic percussion signs. Impaired resonance and slightly increased tactile resistance from the first to the third thoracic vertebra.

CASE IX.—Painful, unproductive cough; restricted respiratory excursion; habitual dyspnea; cardiac hypertrophy: left-sided chronic adhesive pleurisy.

3. *General Thoracic Hyperresonance* (Fig. 8). In the three cases belonging to this group (Cases II, IV, and V) it is fair to attribute the spinal hyperresonance solely to direct conduction of the tracheobronchial tones by the intermediation of the adenoid masses. These were of large size in all three cases, and in none did either emphysema or pleurisy coexist. Dry cough, persistent dyspnea, and great substernal oppression were common symptoms, and hyperresonance of the whole thoracic segment was the common physical sign in these three examples of uncomplicated adenopathy.

4. *Normal Percussion Signs.* In one patient of the series (Case IX, Fig. 9) no impairment of resonance below the level of the third thoracic spine was detected, despite Röntgen proof of the glandular enlargement, and notwithstanding clear mural signs of left pleural adhesions and of cardiac enlargement. Even Ewart's "isolated (ninth) dull spine" was unmistakably resonant, as well as the several processes above it, directly back of the heart and its great vascular trunks. No explanation of the lack of vertebral signs can be hazarded in this instance.

CLINICAL VALUE OF CHANGES IN SPINAL RESONANCE. A review of the foregoing data, considered in the light of results obtained in numerous other mediastinal lesions, warrants the following conclusions as to the clinical utility of vertebral percussion in the group of cases under discussion:

In simple enlargement of the tracheobronchial lymphatic glands percussion of the thoracic vertebræ, especially above the level of the inferior scapular angles, usually affords tonal changes of real clinical value if properly interpreted. These changes, more often corroborative than primarily diagnostic, invariably should be correlated with the mural signs of the individual case.

Hyporesonance with maximum tactile resistance and hyperresonance with minimum tactile resistance may have precisely the same significance in uncomplicated adenopathies. To explain this seeming paradox it is to be assumed that in the former instance the mass exerts a dulling pressure, and that in the latter it conducts the predominant tracheal tone. In glandular enlargements associated with pleuropulmonary lesions, emphysema and pleural adhesions are to be reckoned with as additional factors of hyperresonance and hyporesonance respectively.

In comparison with other (neoplastic) mediastinal masses, tracheobronchial tumors affect the vertebral percussion sound to a minor degree and more often produce dulness than hyperresonance. This general rule has a restricted clinical bearing in bearing in differentiating adenoid and malignant tumors.

In routine examinations ordinary mediate finger percussion is preferable to instrumental pleximeter percussion in studying vertebral changes of sound. The latter method gives no surer clue to tonal changes than that afforded by percussion with the bare fingers, and its practice obviously forbids all judgment of tactile resistance.

THE TRANSMISSIBILITY OF THE LEPRA BACILLUS BY THE BED-BUG (CIMEX LECTULARIUS L.).

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The following paper was presented before the Philadelphia County Medical Society, on April 20, 1912, but publication has been withheld because of a desire on the part of the writers to more

fully study the strain of organisms employed in the transmission experiments, for reasons indicated in the text. Such study has been continued, but a final conclusion has not as yet been attained, although the writers now, as at the time of presentation of the paper, incline to regard the chromogenic acid-fast organisms used in their studies as true leprosy bacilli and to look upon the supposedly contaminating non-acid-fast elements of the same morphology in the cultures as identical, but representing another phase of a pleomorphic organism. A recent statement by Kerr,[1] implicating the bed-bug as a conveyor of leprosy, has led the writers to no longer postpone publication, but to leave to a subsequent time a fuller discussion of the specific status of the organisms employed in their experiments in transmission.

In preface the writers would acknowledge that the uncertainty prevailing in respect to the specific status of various cultures regarded in different laboratories as Bacillus lepræ must necessarily postpone decision as to the value of the laboratory studies in transmission herein recorded. While it is commonly stated that the work of the earlier investigators in attempt to cultivate Hansen's bacillus, employing only the ordinary laboratory media, was without result, it will not improbably be necessary in making up a final decision upon the question of the specific characteristics of the true leprosy organism to carefully review all of their data. The recent workers, however, as Rost[2] and Williams[3] in India, Clegg[4] in Manila, Duval[5] in New Orleans, and others, have uniformly obtained organisms which in the tube apppear as yellow to orange chromogens, which are acid-fast, and which vary in minute morphology from a bacillary to a coccoid form. All of these workers seem to have attained readiness of growth by utilizing culture media in which advanced protein cleavage products constitute an important part, as the extract of putrid fish employed by Rost and by Williams, the medium of Clegg in which by prior seeding with colon bacilli and amebæ the products of hydrolytic splitting were present, the deliberate addition of tryptophane to the medium by Duval, or the preparatory trypsinizing of the medium by the last-named writer and others following him.[6] It is true that certain differences between the strains obtained by these investigators have been urged, but the main features of

[1] United States Naval Bulletin, 1912, vi, 316; reference in editorial in Jour. Amer. Med. Assoc., November 16, 1912, lix, 1798.

[2] British Med. Jour., 1905, No. 2302; Scientific Memoirs by Officers of Medical and Sanitary Departments, India, 1909, N. S., No. 42.

[3] Scientific Memoirs by Officers of Medical and Sanitary Departments, India, 1909, N. S., No. 42.

[4] Philippine Jour. Sci., April, 1909, Series B, iv, 403.

[5] Jour. Exper. Med., September, 1910, xii, 649.

[6] Duval, Jour. Exper. Med., March, 1911, xiii, 365; Smith and Rivas, New Orleans Med. and Surg. Jour., October, 1912.

chromogenic character, acid-fastness in staining and bacillary to coccoid morphology, are common to all of these strains cultivated from leprotic tissue in media having amino-acids as a definite element in their composition in widely separated places by independent workers. No little doubt as to the real status of such growths and the purity of cultures has, however, arisen from the uncertainty of experimental inoculation, and the invariable presence of organisms in the cultures which have been usually looked upon as contaminations or perhaps symbiotic organisms possibly of importance. These are by no means of constant characteristics. They are usually of the same morphology and size as the ordinary acid-fast bacilli, but are non-acid-fast; again, mycelioid growths appear, some acid-fast, some non-acid-fast. (More recently Duval[7] has urged above his original chromogenic organisms a nonchromogenic acid-fast bacillus as more probably the true Bacillus lepræ.) Final determination of both these points is lacking, that is, the verity of existing cultures and question of contamination. In the opinion of the writers there exists an important question in the point raised by Williams[8] as to whether in reality the causative organism of leprosy is not pleomorphic (a streptothrix in his suggestion), with varying phases which include the supposed cultural contaminations. The writers incline to credit this suggested pleomorphism for reasons to be stated elsewhere, and are of the opinion that the cultured organisms used in the following study (one of Duval's original strains) are lepra bacilli, in spite of the fact that in every tube, as demonstrable in stained films, at least a few non-acid-fast organisms of the same morphology as the acid-fast ones were found, and that, moreover, inoculations into guinea-pigs and rats gave but doubtful or negative results. Even, however, should this experimental phase of the study prove valueless because of the employment of bacteria which may eventually be shown to be non-specific, the second phase of the work, inculpating the bed-bug or obtaining lepra organisms when withdrawing blood from a leper, is of interest, and should be recorded.[9]

Laying this problem aside for the time, with clear understanding that in a part of the studies dealt with there is room for legitimate question because of the unproved status of the strain of bacteria employed, a brief discussion of the prominent views upon the mode of acquirement of leprosy is desirable in introduction.

From the earliest references of religious and historical writings to the affection a belief in direct contagion without intermediary has held tenacious sway, personal contamination of the clean by

[7] Jour. Cutan. Dis., July, 1912, xxx, 389.

[8] Indian Med. Gaz., Supplement, May, 1911; see also Deycke, V Internat. Derm. Kongr., September, 1904, Band i, p. 385 (Ref. Centralbl. f. Bakt. u. Parasitenk., xxxvi, 662), and Deycke and Reschad, Deutsch. med. Woch., 1905, xiv and xv (Centralbl. f. Bakt. u. Parasitenk., vol. xxxviii, Ref., 415).

[9] See Kerr, supra cit., and Long, infra cit.

the leper being guarded against by stringent laws. Nevertheless, in modern times the insufficiency of such views has been a marked feature in scientific expositions of the affection; and no man of experience with leprosy today but recognizes the fact that quite commonly long and even intimate association of unclean and clean may fail to establish contamination. Isolated cases in families, sometimes large families closely associated because of crowding of the dwelling, are the rule rather than the exception, and commonly the effort to trace the source and route of infection in such individuals is futile. Under this same heading are ordinarily meant by the populace, and may here be included, infection by actual bodily contact, by special sexual contact, or by contact with ordinary inanimate objects contaminated by a leper, as clothing, common utensils, and similar objects. That occasionally transmission of the causal agent of the disease is in some such manner actually accomplished has certainly not been disproved; and that it may sometimes thus take place may be accepted as a mattter of possibility and probability. But there is little evidence that such direct transmission is the rule. Were it even moderately common, infected families should far more frequently furnish multiple cases than is known; attendants and nurses in leper hospitals should show a higher proportion of infection in their number; the recognition of the source of infection should frequently be possible, and appreciation of the time and mode of transfer should often be clear.

The older conception of the disease clearly included the idea that respiratory transmission is possible, expressions indicating the danger of breathing in the exhalations and atmosphere close about a contaminated subject being not infrequent in the older writings. The clinical observation[10] of the frequent presence of Hansen's bacilli in the nasal and oral mucus lent in recent years some added weight to the revived belief, but again the proposition fails of actual proof. It is altogether probable that there is dissemination of the essential microbes with the nasal and oral discharges to the surroundings of the leper, but we are ignorant of the fate of such discharged bacilli. Were the subsequent step of infection merely that of inhalation the same arguments demanding a probability of more frequent infection of those about leprous subjects should prevail. The appearance of the bacilli in the nasal secretions is really no earlier than in other excreta and in other parts of the same cases; and their early recognition in the former is by no means valid evidence that the nose is the primary point of infection. While the possibility of this mode of transmission cannot be set aside completely, its acceptance can at best be only tentative, and certainly not to the exclusion of other and more probable methods.

[10] Bibliography in Amer. Jour. Med. Sci., November, 1894, p. 541; Sticker, Münch. med. Woch., 1897, No. 39, p. 1063, and No. 40, p. 1095; Schäffer, Arch. f. Derm. u. Syph., xliv, 159.

Even before Hansen's discovery of the bacillus of lepra the chance of acquirement of the disease by alimentation had been proposed. The eating of fish, especially of putrid fish, of spoiled cheese, oils, excessive indulgence in pork, and a variety of other foodstuffs was at one time urged, but always without acceptable data. In the latter part of the past century Sir Jonathan Hutchinson[11] revived the theory of acquirement from the eating of fish, but in spite of his authority and his plausible arguments there was but slight credence yielded to his views. There must be decided satisfaction to Sir Jonathan in the success of Duval and his associates,[12] which the writers do not hesitate to confirm from their experience, in readily infecting fish (in which inoculation with cultures of Bacillus lepræ is rapidly followed by a wide appearance of the acid-fast organisms in the various organs of the body, even though definite nodular inflammatory reactions are not found and the fish remain indefinitely apparently unharmed). It is said that when leprosy is endemic and the drainage carries the discharged lepra bacilli into a quiet sea arm the fish in the latter have been found leprous. The writers are inclined to agree with Couret[13] and Duval that fish and other cold-blooded animals, as turtles and snakes, may represent the true habitat of the lepra bacillus, and that warm-blooded animals, including man, are relatively or absolutely resistant and require either special dosage to insure infection or special natural or acquired predisposition to become leprous after the introduction of the bacilli. That infection from infected and uncooked or inperfectly cooked fish, either from the introduction of the bacilli into wounds of the oral or esophageal mucous membrane made by fish-bones or by gastric or intestinal inoculation through abrasions or absorption, does not in this light seem very improbable. (In a number of carefully studied early cases of human leprosy there has been noted profuse dissemination of the bacilli in the internal organs without focal lesion, as in the spleen and liver, at a time, too, when the skin showed no gross change; which may be an argument to one who does not regard the disease as primarily a general one that primary inoculation was more likely internal than in the skin. For that matter the same suggestion may as well be accepted from the occurrence of the so-called initial fever of leprosy, appearing before any skin lesions are apparent by our present modes of observation.) That popular belief holds that the use of rotten fish is particularly dangerous in this connection is singularly substantiated by the fact that the cultivation of the bacilli of leprosy in the laboratory is favored

[11] Med. Times and Gaz., October 30, 1867; Med. Press and Circ., July 8 and August 11, 1880; Lancet, London, 1880, No. 13; British Med. Jour., March 22, 1890; Leprosy and Fish-eating, London, 1907.

[12] Couret, Jour. Exper. Med., May, 1911, xiii, 576.

[13] Loc. cit.

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[12] Couret, Jour. Exper. Med., May, 1911, xiii, 576.

[13] Loc. cit.

by media containing the products of digestion and cleavage of proteins.

The writers are unwilling at this stage of our knowledge to further advocate the theory of Hutchinson, but believe it worthy of more careful study than has been accorded it in the past; and should the acid-fast chromogenic bacilli here involved actually prove to be the true pathogenic agents of leprosy, would accept the idea as a probability for at least some cases of human acquirement.

Whatever credence may tentatively be granted to any one or all of the suggestions thus far outlined, brief reflection must surely lead to the conclusion that no one, or the whole group together, can satisfactorily explain the acquirement of the affection in all or even in any large proportion of the instances of the diseases in natural conditions. Supposing fish-flesh to be a conveyor of leprosy to human beings, there are nevertheless many localities in which the disease prevails, but where fish constitute only a rare article of diet, if ever used. If respiratory acquirement be possible, it is open to reasonable doubt that this can be a prevailing mode when one recalls the comparative infrequence of infection of relatives and attendants in homes and institutions inhabited by lepers and the common appearance of the disease in persons who do not recall exposure to lepers; and the same statements are *apropos* to the idea of direct contagion.

These evident inefficiencies of the more prominent attempts to explain the acquirement of leprosy, with comparative reflection upon the vagaries of such acquirement, and the peculiarities of insect transmission of a now rapidly lengthening list of diseases, urged upon the minds of the writers the chance of some living and moving agent, as an insect, enacting the role of a transmittor. The idea of possible insect convection is not new, although it was arrived at by the writeres entirely independently. Castellani and Chalmers[14] refer to Nuttall as pointing out that Linnaeus and Rolander regarded a fly (Chlorops lepræ) as the active agent of transmission from one human being to another; that Corredor suspected flies in general; Joly, Sarcoptes scabei; Sommer, mosquitoes. The same writers state that Goodhue demonstrated leprosy bacilli in Culex pungens and in the common bed-bug; and that Marchoux and Bournet suggested some of the simulidæ as carriers of the disease. Walter Brinkerhoff,[15] while Director of the Leprosy Investigation Station of the United States Public Health and Marine Hospital Service at Honolulu, called attention to Goodhue's discovery of the bacillus in the body of Culex pipiens, and to a similar discovery by Mr. John R. Taylor in the stomach of a mosquito which had previously bitten a leper in Las Animas Hospital

[14] Manual of Trop. Med., New York, 1910, 1st ed., p. 839.

[15] Note on Possibility of Mosquito Acting in Transmission of Leprosy, Public Health and Marine Hospital Service of the United States, 1908, p. 23.

in Havana; and comments upon the possibility and possible method of transmission by mosquitoes. After the work of the writers was well advanced the note of E. C. Long,[16] of Basutoland, was encountered by us. Long states that in his study he collected bed-bugs from huts where no leprosy existed and allowed them to bite lepers in the vicinity of leprous nodules of the face. The bugs being killed and the alimentary tract and its contents examined, "in every bug that bit freely a bacillus was found, which in shape, size, and staining reactions is similar to the Bacillus lepræ." He also cites the case of a native of Basutoland, who came from a village free from leprosy and who had no lepers among his relatives, but who in a village fifty miles from his home had spent a single night in a hut from which recently the solitary leper of this second village had been expelled. During this night he was severely bitten by bed-bugs, and within a year the lesions of leprosy appeared upon him.

Impressed with the chance and the compatibilities of the idea of insect transmission (which impression was later confirmed and strengthened by the statements above mentioned) the writers instituted a study to determine the problem. At first, merely as a preliminary observation, it was determined positively that it is possible for ordinary house-flies, carrying the bacilli, as they are known to carry a variety of organisms on the exterior of their bodies, to convey the infection to fresh media. The flies were placed in glass vessels containing various substances, as sugar solution, blood, etc., previously contaminated with lepra bacilli from culture tubes (one of Duval's strains). After the flies had crawled over or through the contaminated material and tasted of it the bacilli were readily obtained both by staining and by culture from the proboscis and from the legs. No evidence was obtained, however, that the bacilli were taken into the alimentary canal of the fly. A number of the insects after having been seen to feed upon the contaminated material were killed, their legs, wings, and heads removed, the exterior of the body well washed in disinfectant solutions, and in the smears made from the thorax and abdomen thus prepared no organisms comparable morphologically and tinctorially to Bacillus lepræ were discovered.

The main investigation was, however, from the first directed to the common bed-bug (Cimex lectularius L.) because of its ubiquity, close relation with man, and its commonly believed but unexplained preference for some individuals and avoidance of others in the same groups. For a long time, beginning in the fall of 1911, attempts to induce the bugs to ingest blood to which bacilli from the culture tubes had been mixed, failed, and at this time there were no lepers available upon whom the bugs could be fed. After

[16] Arch. Middlesex Hospital, Clinical Series, August, 1911, viii, 49; British Med. Jour., 1911, ii. 470; Jour. Trop. Med., 1912, xv, 72.

numerous failures it was found that if the blood (using citrated blood of dogs) with admixed bacilli were placed in a suitable dish and covered with a piece of fresh skin the bugs would bite through the skin and suck up the artificially infected blood.[17] At first dog skin was used, but was found too thick, and rat skin was thereafter employed. With the thicker skin, not easily penetrated by the proboscis of the insect, two bugs out of a dozen were found to contain bacilli; but with the thinner rat skin all the bugs except the very small ones succeeded in reaching the blood and became infected. The hair is shaved off the skin and the latter stretched over the blood in the dish, its under surface in direct contact with the blood; and the dish thus prepared is kept warm in the incubator, the bugs being applied in the incubator chamber under an inverted test-tube. Smears made from the excised alimentary canals of unexposed bed-bugs were invariably free from acid-fast bacilli. Smears made from the bugs immediately after biting, as a rule, showed but few bacilli, and those of the coccoid form which had been mixed with the blood from the culture-tube. From observations made upon over one hundred infected bugs there is no doubt in the minds of the writers that for a time the bacilli increase in size and also in numbers within the bed-bugs. They elongate into typical bacillary form, and in sections of bed-bugs may be found, at least between the third and tenth days after feeding, not only in the alimentary canal but also in the various glands of the head, thorax, and abdomen. They are not numerous in the glands, but in the series examined have been repeatedly found in these locations. After a time they disappear from the bugs, the time of disappearance varying between two weeks and thirty or more days. The mode of disappearance is probably not a simple one, some of the bacilli being found discharged with the fecal matter, others apparently broken up in the bugs into fine acid-fast granules.

After this stage of study had been reached, fortunately for the work, it became possible by the kindness of the staff of the Municipal Hospital for Infectious Diseases, through Dr. J. A. Kolmer, pathologist to the institution, to feed bed-bugs directly from two lepers who had been received in the hospital a short while previously. In smaller numbers, but indubitably, acid-fast organisms of the usual human type of lepra bacilli were found in a number of the bed-bugs which had fed upon these subjects, but not in all. From further study of these human cases the writers are persuaded of the existence in lepers of a true lepra bacillemia, the bacilli being obtained both by culture and by staining (blood citrated, laked,

[17] A personal statement to one of the writers by Professor Nuttall was recently made which easily obviates this difficulty. If the antennæ of the bed-bugs be removed by section with fine scissors or destroyed by a hot point there is no hesitation on the part of the insects to suck in any material offered.

centrifugated, and the sediment spread and stained) in blood removed directly from the veins without contact with the skin lesions. This belief is further urged by the fact that lepers constantly show the organisms in the various secretions and in the internal organs as well as in the dermal lesions. It seems quite possible to think that failure to acquire the organisms by the biting bugs, when it is recalled that similar failures were noted in the laboratory feeding through the thick skin of the dog, may have resulted from mechanical difficulty of penetration through the thick leprous skin to a suitable capillary (the bacilli in the fixed tissues being probably less readily acquired than those in the circulating blood). It is easy to surmise tentatively, in partial explanation of the rarity of infection of entire family groups by bed-bug transmission from a given leper in the family, that only the well-gorged bugs are likely to contain bacilli; that these are not likely to again feed for a number of days, and in the meantime may have lost their bacilli as above shown; that, following the observations above noted, perhaps in not all cases do the bacilli gain access to the salivary glands and tubes of the bugs, and that failure of transmission at the next feeding may sometimes depend upon this feature; and that, therefore, even disregarding possible individual immunity from the bed-bug or special individual resistance to lepra bacilli by given human beings, it is not to be expected that leprosy should invariably follow the bite of a bed-bug which has previously fed upon a leper.

The well-known difficulty and questionable results of animal inoculation thus far reported by various writers have interfered with the determination of the final link of the chain of reproducing the disease in appropriate animals by permitting infected bugs to bite such subjects. Guinea-pigs, Japanese dancing mice, white mice, and monkeys have been employed with varying success by different investigators; and it is well known that among the cold-blooded animals fish, turtles, and snakes have been found suitable subjects for the growth of the bacilli, but do not exhibit histological changes from the presence of the bacilli in the economy. In inoculation studies with mammals in this laboratory guinea-pigs and white rats have been used. Thus far no results whatever have been attained in rats, which apparently are completely immune to the strains of lepra bacilli in our possession, no matter what the dosage. Duval's[18] suggestion that previous sensitization of the experiment animal by injection of dead cultures or the lepra bacillary protein has recently been followed, but as yet no results have been attained either in guinea-pigs or rats. One of two original guinea-pigs inoculated without sensitization last summer with one

[18] Duval, Jour. Exper. Med., August, 1911, xiv, 181; Duval and Wellman, Jour. Infect. Dis., July, 1912, xi, 116.

of Duval's strains showed in the inoculated leg a swollen inguinal gland, from which and from a small nodule at the site of inoculation acid-fast bacilli and lepra cells containing bacilli were obtained when the animal was killed. Of more than twelve warm-blooded animals either directly inoculated or bitten by infected bed-bugs this single successful result can at this time be recorded. Thinking that cold-blooded animals would perhaps lend themselves better for the biting experiments attempts to get the infected bugs to bite fish and frogs have been made; but it has been impossible to induce the bed-bugs to bite fish at positions where scales were removed to permit penetration. Several frogs after many trials were apparently bitten (the bugs puncturing through a bit of rat skin into the frog, but never showing any inclination to feed on the uncovered frog). In none, however, were bacilli found after natural death or after sacrifice.[19]

In despair of actually producing the disease by the bite of infected bugs in the available experiment animals, it was sought to find at least whether in biting there takes place a discharge of the lepra bacilli along with the mouth secretions of the bug into the wound. The tiny site of puncture into the skin of guinea-pigs and other subjects was at once excised for examination. In serial sections of several of these minute bits of epiderm and corium the writers have failed to find any bacilli, but five times in fresh smears of the crushed skin from a group of eleven attempts made in this wise, small bunches of acid-fast bacilli have been found, in four of the five controlled by negative findings in smears similarly made from tissue in the immediate vicinity and from the surface. From their appearance the writers believe these to be lepra bacilli transferred to the experiment animal by the bite of the infected bugs. That no more uniformly successful results have been attained by the writers is not to be regarded a matter of much surprise, as it is to be recalled that at the time of biting there may have been in the oral glands of the bug none of the bacilli, and that further, the technical difficulties in finding the small numbers of bacilli deposited in the line of puncture into the skin are very real; but so far as it goes there seems to us little room for doubt that an actual transference was accomplished.

In conclusion, always with reservation occasioned by the uncertainty of the pathogenic value of the bacilli employed, the matter of these preliminary studies may be summarized as follows:

1. Bed-bugs can be induced by methods detailed to take up lepra bacilli with blood to which the bacilli have been added.

2. Within the bugs for a time the bacilli increase in size and apparently in numbers, but eventually disappear, partly by dis-

[19] All the animals here referred to have remained for months without appreciated infection, and when killed showed no bacilli in spreads from blood and internal organs. This is true of both inoculated and bug-bitten experiment animals save as above recorded.

charge with fecal matter, partly also by disintegration within the bed-bugs.

3. Within the bugs thus infected the writers have found the bacilli in the glands as well as in the alimentary canal.

4. Bed-bugs acquire lepra bacilli also with blood taken from human leprous subjects, but not invariably.

5. Bed-bugs infected in the laboratory, and presumably more certainly and more heavily infected than those which are infected from human beings, may transmit the bacilli by route of the sucking apparatus to the skin of the animal bitten.

6. Whether thus the disease is transmitted in nature, that is, whether the organisms are unchanged and of sufficient virulence to induce leprosy, remains to be proved; and the writers would here also indicate their belief that if bed-bugs really do transmit the disease, as they suggest, they are probably only one of a number of possible conveyors, other types of biting and sucking insects being equally open to suspicion (particularly those which regurgitate in biting).

SYRINGOMYELIA: WITH AUTOPSY FINDINGS IN TWO CASES.

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The development of cavities in the spinal cord following apoplexy, traumatic hemorrhage, myelitis, embolic processes, or primary degenerations of the nervous tissues have not infrequently been described. In a number of instances in which a primary causative factor had been suggested for the condition the authors indicated that an inflammatory process and reactive gliosis had occurred secondary to the development to the cavity. The type of cavity developing in the cord is different in many cases, and this has led to a number of theories concerning the mode of origin. Moreover, the clinical history of the onset of these cases in adults is so divergent that it would appear that more than one factor was concerned in their development.

The majority of cases of syringomyelia have been described in association with gliosis, or as some prefer to call it, a diffuse glioma. Much attention has therefore been concentrated on this aberrant tissue of the cord. True gliomas of the cord without the presence of degeneration and cavity formation are known, while, on the other hand, there have been cases in which the development of a local or extensive cavity in the cord has been unassociated with primary changes in the glia.

The relation of syringomyelia to true tumors is particularly important in those cases where the gliomatous processes can be demonstrated to precede the cavity formation. In these conditions there is a definite mass of invading tissue which extends longitudinally in the cord and commonly involves the gray matter and the posterior columns. It would appear that the growth had its origin in the glia of the gray matter, but its subsequent extension not infrequently invades the white matter of the cord, where it displaces the various tracts.

The involvement is generally greatest in the posterior columns, but the tumor need not be confined to this region. Thus the entire cord may be infiltrated and destroyed in one segment, leaving little or no normal tissue, while in the segments both above and below this area the new-growth is confined to the tissues behind the commissure. At different periods of development the gliomatous mass may undergo softening, with partial absorption of the liquefied area. This softening is usually most extensive in the area of the greatest tumor involvement and in the areas of the cord occupied by the secondary growths. The absorption of the softened matter may lead to the complete disappearance of the cord in one or more segments. In other instances the main gliomatous mass continues to extend almost as rapidly as the central softening, with the result that the cord is occupied by a considerable tumor mass with an inner cavity. From the area of primary softening a similar process of degeneration follows the central portion of the infiltrating gliosis. Thus the column of new-growth occupying the posterior tracts comes to have a tubular cavity passing through it. Where the extension of the gliosis or tumor has followed several nerve tracts there may occur separate channels of softening. The process of softening is also accompanied by degenerative changes of the cells and tissue immediately surrounding the tumor tissue. Several investigators have indicated that the process of degeneration is associated with certain vascular changes as well as pathologic conditions in the enveloping membranes.

Under the general consideration of syringomyelia is included the discussion of cavity formation resulting from congenital anomaly. Such conditions are observed in cases where the spinal canal has been improperly closed, leading at times to the formation of a diverticulum which is still in communication with the spinal canal or where a channel near the posterior sulcus is independent of the central canal, and in no way communicates with it. Cavities of the former type are lined with a layer of columnar cells simulating the ependyma. It must, however, not be inferred that all cavities having such a lining membrane are of congenital origin. Some of the lesions of later life appear to acquire a similar lining.

The cases which are of the most interest are those which develop in adult life or at least in whom the symptoms first appear at this

time. These cases have led to repeated controversies as to the primary factors in their origin.

Although, clinically, a group of symptoms indicative of syringomyelia has been described, not a few cases found at autopsy have presented symptoms of quite another character.

The following two cases of syringomyelia are of interest in indicating the mode of origin of their cavities, in the one case with and in the other without the presence of tumor.

CASE I.—Mrs. R. M., aged thirty-eight years; housewife. The patient was admitted to the Pittsburgh Hospital September 19, 1910, under the service of Dr. J. D. Heard, to whom I am indebted for the clinical history.

On admission the patient complained of pain in the lower abdomen and along the spine, and inability to move the legs. The patient was the mother of nine children, and had been a healthy woman until last fall, when, after nursing her husband through a prolonged fatal illness she broke down. Moreover, at this time a number of subcutaneous abscesses developed in various parts of the body. Associated with this infection she had an acute attack of pain (acute pleurisy) in the left chest, which confined her to bed. She gradually improved, so that she was able to be up until the morning of her admission to the hospital. Suddenly upon that morning she found herself unable to move either leg. She was very definite in stating that this complete paraplegia took place within a period of two or three minutes. Since then the paraplegia has been complete. The patient was an emaciated female. There was a complete paraplegia, with loss of reflexes below the waist line. The bladder was distended to a point about an inch below the umbilicus, and contained 1000 c.c. of urine. Anesthesia was complete to all forms of sensation over the surfaces below a transverse line 3 cm. above the umbilicus. The left pleural cavity was the seat of effusion, which reached to a point opposite the seventh rib posteriorly. This effusion was rapidly absorbed, leaving behind an impaired percussion note.

Nervous System. Complete anesthesia over the area mentioned, which persisted until the end. There was no shifting or extension of the original area. The patient was never able to make the slightest voluntary movement of the legs, but during the last two weeks of her life, involuntary twitchings occurred in the anterior muscles of the thigh. There were marked trophic disturbances. Decubitus appeared over the sacrum about six days after admission. This spread rapidly, the tissue literally melting away. At the time of death ulceration had extended to the bone and measured 10 x 12 cm. There was also one over the inner side of the left foot and also an ulcer over the left hip. Control of the bladder or rectum was not regained. The urine toward the last became excessively fetid.

Laboratory Findings. The Wassermann test for lues was negative. Albumin was constantly present in the urine. From the first, granular casts, pus, epithelial cells, and occasional red blood cells were found. Leukocyte count varied from 12,000 to 21,400.

Clinical Diagnosis. The sudden appearance of the manifestations suggested the diagnosis of hemorrhage into the cord. Death was caused by pneumonia, sepsis, and exhaustion. An autopsy was performed one and a half hours after death.

Autopsy. The body was that of a middle-aged woman, 165 cm. tall. The skin surfaces were pale and the body was considerably emaciated. The pupils were narrow, the right being slightly larger than the left. Extensive and deep decubitus ulceration was seen over the sacrum, which extended to the bone, and measured 10 cm. x 12 cm. A round punched-out ulcer was seen over the left hip, exuding pus. A small fibroma was present in the skin of the right side of the neck. Some superficial ulcers were found over the heels and one over the inside of the foot. The genitals were negative. A small amount of blood exuded from the vaginal orifice. There was no postmortem rigidity of any of the muscles.

Thorax: No excess fluid was found in either pleural cavity. Some old adhesions were seen over the apex of the left lung and along the posterior border of the right lung. On bringing forward the left lung the lower lobe felt solid and was firmly adherent to the posterior thoracic wall. On removal the lung substance was torn by the adhesion. There was some purulent exudate enclosed by the adhesions behind the lung. This exudate was seen to burrow behind the parietal pleura and enter the intercostal space between the eighth and ninth ribs. An opening 1 cm. in diameter was seen in the pleura. Behind this opening was a larger cavity, from which pus could be expressed. This cavity was immediately over the angles of the ribs, and extended up and down, being 7 cm. in length. The ribs which formed the posterior boundary of this cavity were eroded on their inner surfaces. The pus cavity was 4 cm. in width and advanced to the bodies of the vertebræ. The right pleural cavity also showed some dense adhesions behind the posterior border of the lung, while in the retropleural tissues opposite the angles of the seventh, eighth, and ninth ribs was a shallow abscess cavity almost identical in size and appearance to that on the left side. These two abscess cavities had paths of communication across the vertebræ. The eighth and ninth ribs as well as the vertebræ opposite the abscess in the right side were denuded of their periosteum. There was a distinct lateral curvature to the left of the dorsal spine beginning at the seventh dorsal and ending at the first lumbar. The internal viscera showed nothing particularly of interest. A septic pneumonia was found in the upper lobe of the left lung. Extensive suppurative processes were present in the kidneys and urinary tracts.

Cord: On removing the cord some pus was noted about the vertebræ and on the outer surface of the dura in the region of the intervertebral foramina of the seventh, eighth, and ninth dorsal segments. The dura was decidedly thickened in this region. There was no evidence of inflammation nor of pus within the dura mater. The pia was seen to be free from adhesions and exudate. Above the eighth dorsal vertebræ the cord was normal. Opposite the eighth and the upper part of the ninth dorsal vertebræ the cord did not present its normal contour, but instead of being firm and round it was soft and completely flattened. The flattening was due to the loss of the structure within the membranes. The pia mater over this area showed some injected vessels. The cord when cut through at the upper border of the ninth dorsal was disintegrated and structureless, and exuded a yellowish creamy material looking not unlike pus. Sections through the cord opposite the fifth, sixth, and seventh dorsal vertebræ showed the cord structure fairly intact, save for a small circular opening the size of the lead in a pencil, which on pressure exuded a pus-like material from it. There was no evidence of old or recent hemorrhage and no thrombosed vessels were observed. Examination of the pus-like material failed to reveal bacteria, and no cells could be found. The material consisted of a fine debris. Above the level of the fifth dorsal segment the cord was intact. Sections made through the tenth dorsal segment of the cord showed a number of necrotic-looking cavities in the posterior and lateral tracts, which contained a soft creamy debris. Sections through the eleventh segment showed a single cavity in the posterior tracts which only extended to about the middle of the segment. Below this level the cord showed no changes.

Microscopic Examination. Sections made from the eighth dorsal segment in the region of the greatest macroscopic change showed an almost complete necrosis of all structures within the cord. The area formerly occupied by the cord was replaced by a debris contained within the pia mater. Along a portion of the pia and apparently adherent to it was a thin layer of nervous tissue, showing much degeneration. This tissue could also be observed along the anterior sulcus where the pia with the bloodvessels was still intact. The central canal was to be seen and its lumen was patent. There was no evidence of a proliferation of the cells lining the central canal. The gray matter of the cord and particularly the anterior horns could be followed in outline, but showed extensive degenerative changes in its structure. A number of pyramidal cells showing chromatolysis were observed. On the other hand, the tissue of the posterior portion of the cord, including the white matter and the posterior horns, was disintegrated. Within these cord lesions there was no evidence of an inflammatory reaction. Leukocytes and lymphocytes were entirely wanting. Moreover, a careful

study of the sections failed to reveal any evidence of thrombosed vessels within the cord. It was observed that in the small portions of the nervous tissue remaining opposite the severely damaged area the glia cells appeared more prominent than normal. These cells were to be observed as large spherical or at times irregularly shaped structures having very few processes. Some of the cells resembled endothelial cells, save that the nucleus was eccentric and occasional ones had short fibers. These cells were more prominent in the white matter than in the remains of the gray. Sections made through the fifth, sixth, and upper part of the seventh segments of the dorsal cord showed a fairly intact structure, save in the presence of a simple cavity lying immediately behind the commissure and slightly to the right side. This cavity occupied the white matter of the cord, and only bordered upon the gray. The tissue of the commissure was not involved, and although the central canal appeared to be narrowed the cells lining it did not enter into the formation of this cavity. The cavity was irregularly outlined and had no lining membrane. A necrotic wall without inflammation was its boundary. The tissue surrounding the cavity was loose and almost edematous. In places the large spherical glia cell was prominent, and although forming small aggregations, did not develop into masses. An irregular reaction in the glia cells of the white matter was to be observed in different portions of the cord. Immediately external to the posterior horns were seen occasional aggregations of large glia cells, which had developed immediately surrounding the bloodvessels. The diameter of the cavity passing upward toward the dorsal cord was not uniform but varied, at times occupying the entire width of the white matter lying between the posterior horns immediately behind the commissure. A similar but more irregular cavity formation was found in the segments below the level of the main lesions. In the tenth dorsal segment a number of irregular necrotic cavities were found in the white matter of the posterior

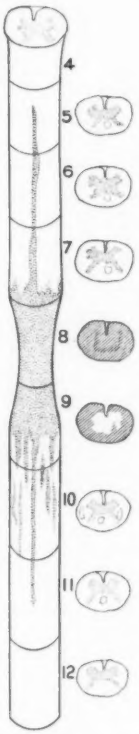

FIG. 1.—Cord of Case I, in which almost complete absorption of the eighth and ninth segment has taken place. A single cavity is seen passing upward, while multiple small cavities pass downward and enter the tenth and eleventh segments.

columns, as well as in the lateral columns. The character of the cavities was similar, in that none of them had a lining membrane, but were bounded by a loose and partly necrotic tissue. In the eleventh dorsal segment a single cavity was present in the posterior columns. In no section was there any association of the cavity formation and the central canal to be observed. Sections of the dura mater showed a considerable thickening of the outer tissues and the presence of an infiltration by lymphocytes and plasma cells. The bloodvessels in the dura were the seat of an inflammatory reaction, but none of them showed a complete closure of their lumina. In only one vessel, a vein, was there found a recent adherent thrombus which was undergoing organization. The vessels lying immediately around the cord in the pia appeared normal.

Anatomic Diagnosis. Acute softening of the cord; syringomyelia; chronic pachymeningitis; chronic localized empyema of the thorax; interstitial abscess of the thoracic wall; unresolved pneumonia, with abscess of lung; old pleural adhesions; acute suppurative cystitis and pyelonephritis; trophic ulcers of skin.

The patient was suffering from a chronic pyemia and empyema in which the suppurative process of the thorax had extended into the spinal column and over the dura at the eighth dorsal segment. A decided inflammatory reaction was present on the outer surface of the dura, but it did not extend within this membrane. The sudden onset of the paraplegia, with complete loss of sensation, suggested hemorrhage or embolism of the vessels of this part of the cord. The microscopic examination showed no evidence of old or recent hemorrhage, and the lesion, which was the seat of extensive disturbance, consisted of an almost complete liquefaction and absorption of the cord structures at about the eighth dorsal segment. This cord destruction gave no indication of a true myelitis, nor was there evidence of new-growth. From this extensive and severe lesion there extended in both directions of the cord, cavities containing a necrotic material and outlined by irregular walls. One cavity extended upward into the fifth dorsal segment, while another passed downward as far as the eleventh dorsal segment. There was no evidence that the spinal canal was in any way involved or associated with the cavities, nor was there an ependyma lining them. In a number of sections a reaction was observed in the glia cells amounting to a proliferation of this tissue in the vicinity of the cavity formation. In other regions, however, changes in the glia were entirely wanting. The cavity formation involved mainly the white matter of the posterior columns.

Case II.—J. H., aged twenty-five years; laborer. The patient was admitted to the Mercy Hospital on January 16, 1912, under the service of Dr. G. O. Goulding. On admission the patient complained of the loss of the use of both lower extremities.

Previous History. About two weeks ago he did not feel well and noticed that his legs felt sore. He was able to walk on January 14 and 15, but on January 15, on attempting to get up in the morning, he found he was unable to walk or stand. He had no indication of the onset of this condition. Closer questioning of the patient revealed no detail of the present illness. He denied having had any accident or acute infection in recent years. At the time of admission there was a complete motor and sensory paralysis below the level of a line situated about midway between the nipple and umbilicus. The anesthesia was complete to all forms of sensation. There was no voluntary control of the sphincters or the bladder. As the patient had to be catherized, and although every care was taken to prevent infection, a cystitis developed about four weeks after admission. Further, large decubitus ulcers developed which were very deep and showed no attempt at repair. The patient gradually became septic, and died three and a half months after the onset of the paralysis.

Clinical Diagnosis. Acute transverse myelitis. Death resulted from sepsis.

Autopsy. An autopsy was performed sixteen hours after death. The body was 161 cm. in length and showed marked emaciation. Over the sacrum and both trochanters there were large ulcerating areas, which extended to the bones, and about 15 cm. of both femurs were exposed. The crest of the left ilium was exposed throughout its whole length. Over the chest and knees small round ulcers were seen.

Brain: The skullcap showed nothing abnormal. The dura was not thickened. The Pacchionian granulations were prominent. The hemispheres were of quite normal appearance on their surfaces. There was no evidence of exudate under the meninges. On opening the brain the ventricles were free from exudate. They were not dilated. The brain substance was a little pinkish, but showed nothing abnormal. The cerebellum was without change.

Cord: On opening the spinal canal no change could be observed about its bony structure or upon the outside of the dura. The dura was of usual thickness and its inner surface was smooth. There was no evidence of exudate upon the meninges. The vessels of the pia were injected along the posterior surface. The entire cord appeared swollen and larger than normal. The pia-arachnoid was tense and appeared to be stretched over the cord. In several places where the pia was slightly torn the cord substance bulged outwardly. The most marked change in the cord was between the seventh and eighth dorsal nerves, where there was an area of extensive softening which extended in both an upward and downward direction. Taking the middle point of the softening as existing between the seventh and eighth dorsal nerve roots, the softening of the cord, which involved the entire structure, extended 3.5 cm.

in both directions, in which no structure could be made out. Smears from this softened material showed debris without the presence of any leukocytes. A greater or less change was to be noted in all portions of the remaining cord. Opposite the fifth dorsal vertebræ the cord structure was altered and showed the presence of a softer and whiter area occupying the posterior horns and all the tissues lying between them. What remained of the cord in this area was congested. At the level of the sixth dorsal a similar whiter and softer area was found, but here it was of greater extent. In this region the right anterior horn was also involved by the presence of new-growth. Similar areas of change were noted in the portion of cord below the softened tumor mass. At the upper extremity of the lumbar enlargement the cord was much congested and its markings indistinct. Here, again, however, the posterior portion of the cord was affected. In the pia, at about the tenth dorsal, was seen a small, flat, calcareous plaque.

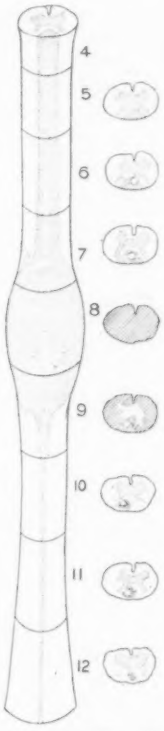

FIG. 2.—Cord of Case II, showing a gliomatous mass occupying the eighth and a part of the seventh and ninth dorsal segments. From this tumor a linear tumor mass passes upward and downward in the posterior columns. Within this extension of the tumor is found a process of cavitation.

Microscopic Examination of the Cord. Sections of the most involved portion of the cord showed a tissue in which normal cord structure could no longer be discerned. The tissue was composed of a fine reticulum and many irregularly distributed nuclei. In the reticulum there was a fine debris looking like degenerated reticular fibers. The nuclei were round and a little smaller than those of lymphocytes. Ganglion cells could not be found. In this tissue the reticulum appeared looser and almost vacuolated, as if a process of degeneration were present. There was, however, in this main tumor mass no evidence of cavity formation. This tissue occupied the entire cord at the level of the eighth segment. In the lower portion of the ninth segment a similar reticular tissue occupied the posterior columns and to a certain extent the lateral tracts. The gray matter was also encroached upon and its outline irregular. What remained of the white matter of the cord was much vacuolated and loose. The tissue occupying the area

between the posterior horns showed evidence of degeneration and necrosis. Thus a mass of necrosis lay within the new-growth occupying the posterior columns. The new-growth could be followed through the succeeding segments of the cord down to its extremity, and within this area an irregular cavity of varying dimensions was present. In the lowermost segment of the cord the cavity was quite patent without the presence of the necrotic island observed elsewhere. The distribution of the tumor mass in the lower cord varied at different levels, but the main portion was found to occupy the posterior columns. The gray matter was variously involved. In the portion of the cord above the main tumor the invading glial tissue had followed the posterior columns. In places, however, other tracts were also invaded, but without any regularity. The invading tumor consisted of a loose reticular structure in which masses with more closely aggregated nuclei were observed. The tissue appeared quite vacuolated. This appearance was more apparent than real, in that many of the tumor cells were composed of large spherical cells with finely granular protoplasm. The reticulum consisted of fine threads associated with smaller cells with dark-staining nuclei. The tissue of the new-growth was quite vascular. The central canal showed a close aggregation of its nuclei and an apparent closure of its lumen. Opposite the eighth dorsal segment some tumor mass was also found in front of the right anterior horns. Extending through the tumor mass and always lying posterior to the commissure was a cavity which began in the seventh dorsal region and extended as high as the lower border of the fifth segment. This cavity had an irregular outline, with necrotic borders. Tumor tissue formed its outer boundary. There was no limiting membrane and tissue debris was found within. The bloodvessels in the vicinity of the tumor or of the cavity showed no evidence of thrombosis and no particular change was to be noted in the vessel walls. In some instances the coats of the small arteries appeared somewhat loose. New bloodvessels with thin walls were evident in the new-growth. In the sixth dorsal segment was found a small cavity isolated from the previously mentioned posterior channel, and apparently having no connection with other openings. This cavity formed an isolated area of degeneration in a small tumor mass, lying in the lateral tracts. The tumor which extended along the posterior columns was more extensive and far-reaching than the cavity formation.

Anatomic Diagnosis. Glioma of the cord with softening; syringomyelia; acute suppurative cystitis; pyelonephritis.

In the second case we are dealing with a man who previous to the onset of the present condition suffered no ill health or accident which might be associated with the lesion in the cord. Without any warning he suddenly found himself completely paralyzed

from the waist down. The paralysis was permanent, and with it extensive trophic ulcers as well as sepsis, beginning in the urinary tract, led to his death some months later.

At autopsy a complete transverse destruction of the cord due to the invasion of a soft glioma was found. This new-growth not only occupied the original diameter of the cord, but even led to a tissue mass considerably greater than the diameter of the cord. This new-growth was situated at the eighth dorsal segment, and from this region the new-growth extended both upward and downward along the posterior tracts. It was in this new-growth that cavities developed by a process of degeneration.

In comparing our two cases it is evident that the cavity formation in the one is entirely different in origin from the other. In each instance, however, it is evident that the development of the cavity had been the result of a necrotic process and that the presence of the channels had in no way been related to the structures forming the central canal. In each instance the wall forming the cavity was ragged and formed by degenerated nervous tissue.

Moreover, no evidence could be found that hemorrhage played any part in the formation of these cavities. In fact, in neither case was there old or recent hemorrhage present.

The question which is of greatest interest concerns the way in which progressive cavity formation may take place in the cord. In considering the cases immediately under discussion we need hardly consider the question of syringomyelia occurring from anomalies of development. Such cases have been discussed by Virchow, and later enlarged upon by Seiden. It is of interest, however, that these authors believed that at times congenital cavities of the cord were followed by hemorrhage and softening as well as new development of glial tissue which would make them simulate the acquired types of the disease. It would, however, be preferable to retain the term hydromyelia for those cases in which the cavity had a development associated with the central canal.

Langhans offered an explanation for those cases in which the central canal alone was dilated. He believed that the process was the result of blood stasis in the posterior part of the skull which led to a venous hyperemia of the cord. The condition therefore simulated a transudate due to passive congestion. Under some conditions the process might later develop into a diverticulum.

The same view was held by Kronthal, who, however, indicated that the condition of passive hyperemia occurred in connection with processes within the spinal column as tumors, chronic meningitis, meningeal adhesions, or compression of the spinal cord. In general the theory of hyperemia found few supporters. Others have indicated that there was a relation between inflammatory thickening of the meninges and the development of cavities in the cord. Thus cases of acute cerebrospinal meningitis, with subse-

quent syringomyelia, are described (Saxer), while Phillips and Oberthur brought forward evidence showing the simultaneous development of thickening of the dura and cavitation of the cord. In many of the reported cases of syringomyelia there was an associated spinal pachymeningitis, but its direct etiologic bearing on the cord condition is far from clear. In our first case a similar association was present, but here the pachymeningitis was clearly the result of an external inflammatory process, while the leptomeninges were not involved. The association of two conditions appears in this case coincident and not directly related. Moreover, autopsies not uncommonly reveal pachymeningitis, adhesions of the membranes, and various lesions of the cord without the process of spinal cavitation.

In those cases of hydromyelia in which the condition is one of dilatation of the central canal there is evidence of a secondary compression and atrophy of the surrounding nerve structures. In the majority of cases of syringomyelia symptoms of this character are entirely wanting.

According to Joffroy and Achard, syringomyelia bears no relation to hydromyelia nor to conditions arising from the central canal. They believe that it arises from chronic inflammatory processes in the gray matter of the cord, which later give rise to cavity formation. The destruction of tissue is particularly associated with circulatory disturbances, probably thrombosis.

The most widely accepted theory of the process is that of Simon and Schultze, which indicates a primary growth of the ependymal and peri-ependymal tissues of the character of gliosis. This development of new tissue progresses along the cord, while a necrosis with subsequent cavity formation develops in the inner and older portion of the growth until the true nature of the tissue can only be observed in the peripheral and distal portions. In some places the nature of the growth indicates a true glioma, and Weigert believes that a differentiation can be made between gliosis and glioma. Occasionally a communication may develop between the cavities of the new-growth and the central canal.

A number of cases of gliosis without the presence of tumor in the posterior columns of the cord have been described. Oppenheim discussed a case under the name of gliosis spinalis in which the symptoms had been those of tabes. The process extended from the cervical to the lumbar cord and occupied mainly the posterior portion of the gray matter. Here and there this tissue contained small lumina.

Against the contention that tumor development always precedes the formation of the new cavity in the spinal cord, Gerlach indicated that some cases showed no evidence of enlargement of the cord as we would expect from tumor, nor did the cord show the usual areas of softening as is seen about gliomas. The irregular

position of the cavity as it occurs in different cases does not permit a common theory of origin.

However, it cannot be denied that in some instances the cavity formation was preceded by true tumor of the nature of glioma. This has been the condition in our second case. Thus we find the undoubted presence of a localized glioma which has increased the diameter of the cord and which in its oldest part has undergone softening. In the main tumor a cavity cannot be distinguished, and the whole mass is so soft that it cannot be handled without producing artefacts. In the further extension of the tumor, central liquefaction with partial absorption has given rise to cavity formation. Thus we have a well-marked glial tumor with secondary cavitation. But, on the other hand, there are cases in which the development of the cavity precedes a glial proliferation, while in a certain group of cases it is impossible to say from the nature of the tissue whether we are dealing with a glioma with extensive cavitation or with a primary syringomyelia having a considerable secondary gliosis.

Within the true tumors the thin-walled bloodvessels are prone to give rise to hemorrhage. At other times the vessels in and about the tumor undergo degeneration, with partial occlusion of their lumina. In these cases central necrosis of the tumor, with cavity formation, is not uncommon. It has been indicated by some that in the early stages of such tumor development, and before definite symptoms have arisen, there is a considerable chance of hemorrhage from trauma which otherwise would have been without harm.

Instances in which cavity formation had occurred subsequent to traumatic hemorrhage within a tumor have also been described.

On the other hand it is evident that cavity formation develops in the cord unassociated with tumor and apparently arising from varied processes. Thus it has been indicated that through primary hemorrhages, cystic cavities may develop, and that a not important cause for the long narrow channels is a progressive necrosis resulting from local vascular or circulatory disease (Westphal).

Thus we find that cavities may be present in the spinal cord under different conditions. These different forms are to be distinguished from each other as having a different mode of origin:

1. *Neuro-epithelioma Gliomatosis.* This is a true tumor having its origin in the cells lining the central canal. The tissue of the tumor is composed of glial cells with a fairly dense reticulum in which are distributed gland-like elements with lumina of different sizes (Rolly, Schultze, Kahler, Schlesinger, Ribbert, and Wright). Babes has indicated that the cells of the central canal sometimes show an inherent tendency to proliferate, giving rise to the ependymal adenomas. Hutchinson suggests that his second case, in which only a small cavity with an epithelial lining was found, had

its origin in some misplaced ependymal cells which under certain vascular stimuli had developed into a cystic cavity.

2. *Diverticula of Central Canal.* A number of cases have been described in which an accessory canal communicating with the central canal of the cord has been found. These accessory channels are lined with the ependymal cells continuous with those in the central canal. The process is probably a congenital anomaly of defective closure (Jacoby and Kahler).

3. *Anomalies of Closure of the Posterior Sulcus.* At times a channel has been observed lying posterior to the commissure and having its walls composed of connective tissue. Some of these channels have been found to communicate with the surface, and it has been indicated that they result from an improper closure of the posterior sulcus in which some of the external membranes have been included (Jacoby, Gerlach). Thomas and Hauser's case probably belongs to this class.

4. *Degeneration of Gliomas.* The greatest number of cases of syringomyelia have probably been described under this class. It has usually been considered that the formation of a cavity within gliomatous tumors has been the result of necrosis from inadequate nutrition or of hemorrhage into the tumor, with subsequent absorption. Such cavities have a necrotic border of tumor tissue without a definite limiting membrane to the cyst. These tumors advance either along the gray matter or along the nerve tracts of the cord. This longitudinal growth may be rapid and the process of cavity formation within the tumor follow closely upon the development of the new-growth. Hyaline and other changes have been described in the walls of the bloodvessels of the tumor, and it has been assumed that these are predisposing factors for subsequent necrosis or hemorrhage.

5. *Primary Syringomyelia.* This class is a comparatively small one and includes those cases in which the cavity formation preceded a gliosis in the cord. In some instances the amount of change in the glial tissue was comparatively slight, while in others regenerative changes were extensive throughout the cord. The processes leading up to the formation of such cavities within the cord are various. Hemorrhage from trauma or spinal apoplexy (Kienboch, Brasch, Westphal, Spiller, and others), thrombosis or embolism of the spinal arteries (Chiari), venous and lymphatic stasis, acute toxic degenerations, changes in the spinal meninges (Japha, Oppenheim), leprosy (Dyer), an occulsion of the spinal canal have each been described as causative factors. As, however, the condition primarily bringing about the lesion in the cord does not lead to the death of the patient, the time that intervenes from the onset of the condition to the death of the patient permits of such further pathologic changes in the cord that a definite statement as to the initial cause of the lesion is often difficult to make. Thus, for

instance, in our first case the clear-cut history would point to embolism or thrombosis of the vessels of the eighth dorsal segment (hemorrhage of the cord having been ruled out by the microscopic findings), and yet there is no positive microscopic evidence to establish the proof. The extensive softening occurring in the cord at the site of primary damage had also destroyed the contained vessels.

An examination of the tissues of this case also indicates that the cavity in the cord became progressively larger and that it continued to extend longitudinally. In other words the entire cavity did not develop at one and the same time. Why, by a process of necrosis and without the presence of an infiltrating tumor, such a cavity should continue to extend through the length of the cord has not been fully explained. It would appear that the process is intimately associated with the blood supply and the vascular anastomosis. In those cases where the spinal arteries have been occluded by embolism or thrombosis it is probable that thrombi continue to extend into the smaller branches and anastomoses of a particular region of the cord, and depending on the extent of the vessels involved, there develops a progressive necrosis with cavity formation.

The reaction occurring in the glial tissue in these cases of primary syringomyelia resembles an irritative hyperplasia. The irritant, probably the products of tissue degeneration, is too slight to lead to an inflammatory reaction, while, however, the cells of the immediate neighborhood respond in proliferation. Similar reactions in the glia are to be observed in the vicinity of cerebral hemorrhages.

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MODERN GENITO-URINARY DIAGNOSIS AND TREATMENT, WITH REFERENCE ESPECIALLY TO LABORATORY METHODS.[1]

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The scope of the subject of this article is so extensive as to make its complete portrayal, in any form other than a book, an impossibility. Consequently, I shall be content to discuss, in a cursory manner, merely the more important advances, diagnostically and therapeutically, that have marked the progress, in recent years, of genito-urinary surgery from the laboratory and endoscopic standpoints. In order to systematize my remarks, the urogenital system will be considered in turn under its anatomic parts—the urethra, the prostate and seminal vesicles, the vasa deferentia, epididymites and testicles, the bladder, the ureters, and the kidneys, with an appendix delegated to syphilis.

The Urethra. Irrespective of the value incident to the routine bacteriologic and cytologic examination of every urethral discharge, it should be a fundamental law, with imperative obligation on the part of each clinician, to investigate immediately, definitely, and precisely the source of any urethral discharge, whether blood or pus, not known absolutely to originate from the urethra. From this obvious professional duty any digression is not only inexcusable but decidedly reprehensible. Those incipient cases of renal tuberculosis, neoplasm, and vesical papilloma which Nature has provided with that initial distress signal, the red blood corpuscle, and which are treated lightly by the administration of a urinary antiseptic under the guise of that too frequent diagnosis and very rare condition, essential hematuria, for a few weeks or months, during which period the lesion not uncommonly progresses to the inoperable state, are observations and experiences unfortunately too well known to us all.

Glass Tests. The time-honored two-glass and three-glass tests, Kollmann's five-glass test, and Young's seven-glass test not infrequently subserve a useful purpose in clinical urinalysis, but it must be remembered that any "glass test" is fallible and commonly leads to inaccurate diagnosis. Nevertheless, routinely, they are of considerable practical utility, with proper interpretation.

I wish particularly to invite attention to a *seven-glass test* which will prove of value in the differential diagnosis of the origin of

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urogenital pyuria and hematuria, especially as a temporary procedure in the absence of those more exact instruments, the cystoscope and urethroscope. The test is performed as follows:

1. The anterior urethra is thoroughly washed out with normal salt solution or distilled water, employing the common glass dressing or piston syringe, or a catheter of medium size. This washing constitutes glass No. 1.

2. Glass No. 2 is a continuation of this irrigation, and serves as a control to prove whether or not the first washing was complete.

3. Glass No. 3 is a partial voluntary urination by the patient, and contains any pus, blood, or exudate originating from the posterior urethra, its appendages, and the higher urologic system.

4. Glass No. 4 is a continuation of No. 3 and serves as a control of its predecessor. It contains only that part of any posterior urethral contamination which may have leaked back into the bladder or originated from the bladder and kidneys; if the posterior urethral exudate is scanty and the higher urinary tract is normal the urine will appear clear.

5. Glass No. 5 contains that portion of urine voided after massage of the prostate and seminal vesicles, and serves to determine the condition of these organs.

6. Glass No. 6 is a continuation of No. 5 and serves as a control of the same, in order to determine whether or not the posterior urethra has been thoroughly cleansed of the secretion and exudate expressed from the prostate and seminal vesicles.

7. Glass No. 7 contains the final urination and indicates the character of urine contaminated by any lesion of the upper urinary tract, as the bladder or kidneys. Glasses Nos. 6 and 7 both may contain material expressed at the time of prostatic massage which has leaked back into the bladder. Comparison, however, with No. 4 will readily reveal the true nature of the vesical urine.

Thus observance of the seven glasses may permit of the following deductions:

Anterior urethritis = exudate in glass No. 1.

Posterior urethritis = exudate in glass No. 3, or glasses Nos. 3, 4, 5, 6, and 7; if in the latter series, it is most marked in No. 3.

Prostatitis or prostatitis and seminal vesiculitis = exudate in glasses No. 3 or 5, or Nos. 5, 6, and 7; in any event it is most conspicuous in No. 5.

Cystitis = exudate evenly distributed in glasses Nos. 3, 4, 5, 6, and 7.

Ureteritis and nephritis = exudate evenly distributed in glasses Nos. 3, 4, 5, 6, and 7, or most marked in No. 7.

In discussing the glass tests a word of caution must be dropped relative to the inaccuracy of that most frequently employed of all, the two-glass test. The urethroscope has demonstrated that

in chronic urethritis the apparent information thus yielded is invariably erroneous; the second glass is seldom pussy or shreddy, unless the posterior urethral exudate is sufficiently profuse to leak back into the bladder.

Diagnosis and Treatment of Gonorrheal Affections. The differential diagnosis between gonorrheal and non-gonorrheal inflammation of the urethra rests ultimately upon bacteriologic study. No longer does the demonstration of an intracellular, Gram-negative diplococcus substantiate the diagnosis of gonorrhea. Indeed, in medical jurisprudence and the courts of justice today, in order to render the evidence legal, the gonococcus must be culturable. Irrespective of the law of the land, bacteriologically, if the identification of the Neisserian diplococcus depended upon its culturability there would exist few cases capable of the diagnosis of gonorrhea. The culture medium which we have found best adapted for the growth of the gonococcus is one prepared from the formula of Dr. John C. Torrey. It consists of the addition of one part of rich ascitic fluid to three parts of meat-infusion peptone agar with 2 per cent. glucose, after the latter has been titrated to about +0.8 to phenolphthalein. Again, the differentiation between the Diplococcus gonorrhœæ and Micrococcus catarrhalis by stained smear is an impossibility; both are Gram-negative and morphologically identical. Culturally the distinction is readily determinable.

Eosin-azur Stain. It has been pointed out that even the Gram-differential stain may fail in the identification of the gonococcus. Routinely many simple stains have been and are utilized for the demonstration, practically, of the diplococcus of Neisser. I wish to call attention to one which in my opinion is most meritorious: One tablet of the commercial eosin-azur is dissolved in 5 c.c. of pure methyl alcohol. A thin film coverslip smear of the suspected material is prepared and dried in the air. A given number of drops of the stain, sufficient to cover the smear, are placed on the coverslip for one to two minutes; to these are added twice the number of drops of distilled water and the whole permitted to stand five additional minutes. The coverslip is then passed through the distilled water, dried, and mounted. The stain is differential to the degree that the gonococci appear as dark blue bodies, the nuclei of the leukocytes as a purple, while the protoplasm assumes a faint blue color. Thus the gonococci are very conspicuous and readily distinguished.

Gonococcus Complement-fixation Test. Schwartz and McNeil continue to assert the increasing value of the complement-fixation test for the diagnosis of gonorrheal infections. They assert that a positive reaction denotes the presence or recent activity in the body of a gonorrheal focus; a negative reaction, however, does not exclude gonococcal infection. A positive reaction is not obtained if the disease is limited to the anterior urethra, nor is it to be ex-

pected earlier than the fourth week, and then only in the event of an acute infection or complication. A positive reaction may persist seven or eight weeks after the pronouncement of cure, and means that the patient should be regarded as still harboring gonococci. About 30 per cent. of cases, clinically considered as post-gonorrheal, demonstrate a positive reaction. Approximately 55 per cent. of patients suffering from chronic prostatitis within three years of the gonorrheal infection give positive reactions. About 13 per cent. of patients supposedly clinically cured for a period of three months exhibit a positive reaction. In women positive reactions are rarely obtained unless the cervix has been involved. In the future it seems logical to infer that more may be expected of this test gynecologically, and also relative to cure and the matrimonial fitness of candidates.

Bacterins and Sera. Although the employment of Neisserian bacterin in gonorrhea seems to be more or less definitely limited, I have repeatedly been able to diagnosticate correctly a synovitis or arthritis, indefinite as to etiology, by the hypodermic administration of large-sized doses of gonococcus bacterin, eliciting thereby a local reaction, analogous to the tuberculin test for tuberculosis. Therapeutically in acute chronic gonorrheal urethritis and in the common complications other than synovitis and arthritis the bacterin has proved of little or no value, although we are as yet unprepared to express final opinion as to its possible value in lessening stricture formation. On the other hand, in joint complications and vulvovaginitis of children, it has been signally meritorious. It is generally acknowledged that gonococcus bacterin has been a failure in the treatment of prostatitis, seminal vesiculitis, and epididymitis. I believe the explanation of this is apparent in the fact that these complications are almost invariably the result of superimposed mixed infection. Naturally a gonococcus antigen will be futile against infections due to the Micrococcus albus, candicans, or catarrhalis, the Streptococcus pyogenes, the colon bacillus, etc. On the contrary, I have been convinced many times that the preparation and administration of an autogenous bacterin, as an accessory therapeutic agent, has materially shortened the convalescence in these patients.

Antigonococcic serum prepared in accordance with the work of Rogers and Torrey for the treatment of synovitis or arthritis and systemic gonorrheal involvement is unquestionably the remedy *par excellence*, superseding in promptness and effectiveness Neisser bacterin. The initial dose should be from 2 to 4 c.c. injected subcutaneously on the peripheral side of the joint.

With respect to bacterins and sera it must be emphatically stated that there are no agents in modern therapeusis more abused than these biologic products. At all times it must be remembered that with careless or improper administration they may be more

potent for evil than for good. Finally they are to be regarded simply as accessories to Nature, not "cure-alls."

Urethroscopy. Mechanical improvements during the past few years in the construction of urethroscopes and cysto-urethroscopes have materially enhanced the utility of these instruments both for purposes of diagnosis and treatment. By their employment anterior and posterior urethritides are accurately differentiated, granular patches located for topical applications of silver nitrate, papillomas diagnosticated and destroyed by the high-frequency current, disease of the veru montanum precisely studied, cysts and papillomas of the internal vesical sphincter defined and treated, infections of Littre's glands and para-urethral abscesses discovered, incised and evacuated by direct endoscopy, the orifices of fistulas and false passages definitely located, and finally protruding median prostatic lobes and bars excised or punched out.

THE PROSTATE AND SEMINAL VESICLES. *Bacteriological Examination.* For the sake of convenience, and because often it is impossible to examine one without molesting the other, these organs will be considered together. Inflammation, whether parenchymatous or interstitial, circumscribed or diffuse, is the commonest of all diseases to which they are subject. As a rule the clinical symptomatology in conjunction with rectal palpation suffices to establish the diagnosis of prostatitis. There are, however, countless cases in which the microscopic examination alone of the secretion and exudate, expressed by massage, will demonstrate the presence or absence of inflammatory disease. Frequently it is found that a markedly cloudy urine filled with flocculent material of a dirty grayish color upon microscopic examination consists exclusively of normal spermatic fluid. On the other hand an opalescent urine, after prostatic massage, evidencing, microscopically, a normal state often reveals by the microscope quantities of pus cells. The practice is universal, yet how many physicians resort to the microscope together with prostatic massage before discharging their patients with gonorrheal urethritis?

The microscope in addition to the demonstration of pus may reveal the presence of bacteria as the gonococcus, the tubercle bacillus, and other pyogenic organisms. Should it fail the exudate may be, and under certain conditions must be, cultured. If tuberculosis is the suppository possibility the suspected material should be injected into guinea-pigs by the Block and intraperitoneal methods.

Since the bacteriologic and immunologic side of this subject must be considered in greater detail in the discussion I have only to remark that it has been my experience that much may be expected from the proper employment of autogenous bacterins in many cases of suppurative prostatitis and seminal vesiculitis.

Microscopy. Finally the microscope is of paramount importance in the examination of spermatic fluid to determine its normal or abnormal character, the presence and viability of spermatozoa, with respect to sterility and the identification of the characteristic dark brown crystals by the use of Florence's reagent in certain medico-legal problems.

Cysto-urethroscopy. It is generally recognized that the sago or tapioca bodies commonly seen in the urine after prostatic massage have their origin from the seminal vesicles. Occasionally these characteristic masses are dirty gray or brownish in color, incident to inflammation of the vesicles. The diagnosis may then be confirmed by the microscope, or if the expressed material is purulent, posterior urethroscopy will frequently reveal pus casts exuding from the ejaculatory ducts or an exudate filling the utriculus.

The cystoscope or, better, the cysto-urethroscope serves, furthermore, a not unimportant sphere of usefulness with respect to the prostate. Its value in the diagnosis of the character and degree of intravesical enlargement of this gland is too well known to require comment at this time; its value in the determination of associated bladder conditions as calculus and tumor, the relative enlargement of the lateral and median lobes, or the mere presence of a median bar or valvular lobe obstructing the internal vesical sphincter, are considerations inducing the twentieth century genito-urinary surgeon to think twice before adopting the perineal, suprapubic, or endo-urethral procedure of prostatectomy.

THE VASA DEFERENTIA, EPIDIDYMITES, AND TESTICLES. *Bacteriology and Serology.* Although certain bacteria, notably the Bacillus tuberculosis, may be identified from the urine voided per urethram, in the case of disease of the vas, epididymis, or testicle, laboratory methods other than the histopathologic have little to offer with respect to the diagnosis and treatment of affections of these organs. I shall allude merely to the value of the Wassermann reaction, to be discussed later, and the employment, diagnostically and therapeutically, of tuberculin.

Tuberculin. With respect to the use of tuberculin, diagnostically, I desire to state that not only here, but generally, I have never been misled by the disclosures of this test. With the possible exception of children and patients with a temperature over 100° F., or in the last stages of disease, the subcutaneous method is unquestionably the least fallible. In children and certain febrile cases the von Pirquet method may be more desirable. I have found Old Tuberculin the preferable preparation for the purpose, and administer as an initial dose 0.5 mgrm., increased if necessary in a series of four inoculations to 5 mgrms. Too much stress cannot be imposed on the fact that a positive reaction depends upon both a general (rise of 1° in temperature) and a local response for the diagnosis of a suspected local tuberculosis. I have seen cases of

epididymitis following gonorrhea in which the current etiologic bacterium was impossible of determination, correctly diagnosticated by the use of tuberculin and subsequently markedly benefited by the administration, therapeutically, of the Bacillen Emulsion preparation.

THE BLADDER. The bladder may properly be regarded as the bureau of information for tuberculosis of the urogenital system. It is undoubtedly well recognized that the tubercle bacillus may invade the bladder from contiguous disease of the prostate, seminal vesicles, and even from the epididymis and testicle; but it is unquestionably too little recognized that one of the most important, frequent, and often earliest symptoms of renal tuberculosis is vesical irritability.

Bacteriologic Examination of Urine. The differentiation of tuberculosis from other pyogenic infections of the bladder is readily possible, microscopically, culturally, or by animal inoculation; and the determination as to the primary or secondary site, and if the latter, as is almost invariably the case, of the original focus of the disease, is usually promptly disclosed by cystoscopy, with or without ureteral catheterization and bacteriologic examination of the collected urine.

Although the dictum of Rovsing that pyuria in the absence of the common pathogenic bacteria means tuberculosis, which fact may readily be established by the microscope and cultural procedures, the absolute and final diagnosis depends upon animal inoculation with the sediment from a twenty-four-hour specimen or urine. Two methods are in vogue. The older intraperitoneal injection of guinea-pigs has been largely superseded by the Block or inguinal subcutaneous method, by which technique the findings seem to be just as accurate and the time of determination of the result shortened from three to six weeks to seven to ten days.

The Cystoscope. The invention that has accomplished most for the advancement of urology and has succeeded through its modern perfection in elevating genito-urinary diagnosis and treatment to a plane second to none in surgery is the cystoscope. Indeed in no system in the human organism is diagnosis possible with equal exactitude.

The types of the cystoscope are manifold. Briefly they may be classified according to purpose, as simple examining, ureteral catheterizing and operative, including both the vesical and urethral or cysto-urethroscope; in accordance with construction, as simple tubular and lens and prism system, including the direct and indirect types with or without corrected image, embodying the right angle, oblique forward and retrograde vision; and finally with respect to manner of employment, whether with air or water distention of the bladder. Each cystoscopist will have the greatest satisfaction and obtain the best results with that type of instru-

ment with which he is most familiar. All things being equal, however, it is my belief that the instrument *par excellence* both for patient and doctor is the water cystoscope, constructed on the evacuation-irrigation principle with the indirect vision lens and prism system

Respecting treatment of certain definite vesical conditions the cystoscope today plays an important role. Cauterization and snaring of endovesical growths, as papillomas, have been practised successfully ever since their first performance by Nitze.

High-frequency Desiccation. During the past two years the application of the Oudin high-frequency current promises to eclipse the older endovesical methods, which are open to the same objection as incisional treatment—namely, that often they invite metastasis or recurrence. Even though recurrence may occur following high-frequency coagulation or desiccation, erroneously styled fulguration, the patient is amenable to a repetition of similar treatment, a procedure seldom tenable with the scalpel; moreover, the organic condition of the patient may forbid general narcosis. The technique requires no special instrument other than a high-frequency machine, the electrodes used consisting simply of insulated wires, manipulated through the ordinary ureteral catheterizing cystoscope.

The Lithotrite, the Cystoscope, and the Rongeur. Litholapaxy as devised by Bigelow was intended to and successfully superseded lithotrity. Today no litholapaxy should be considered complete unless supplemented by cystoscopy to determine the total removal of all calculous fragments. Instruments have been devised combining lithotrite with cystoscope, but they have not yet reached perfection. However, I have found the cystoscopic rongeur of Young of considerable value. By its use calculi protruding from the ureteral orifice, stones free in the bladder, and not over 1 c.c. in diameter, and certain foreign bodies are removed through the male urethra. The blades are not powerful enough to crush any save very soft calculi.

THE URETERS. *Ureteral Catheterization.* Primary disease of the ureter rarely occurs. Usually the lesion, whether infection, dilatation, angulation, or stone, is secondary to some renal, vesical, urethral, or extra-ureteral condition. Nevertheless the ureter becomes the object of certain mechanical procedures, either because of its own disease or that of the associated kidney. Most notable among these is ureteral catheterization. It has many indications: (1) to determine the patency of the canal or the nature of obstruction whether stone, stricture, or extra-ureteral pressure; (2) for the collection of urine directly from the kidney for bacteriologic, cytologic, and other examinations, in the differentiation of renal from other disease lower in the urologic tract and for the determination of unilateral or bilateral affections; (3) for the purpose of

lavage of the renal pelvis; (4) for the introduction of radiographic catheters or bougies in the determination of the position of the ureter relative to the *x*-ray shadows of calculi, calcified lymph nodes, phleboliths, etc.; (5) for the purpose of collargol and other silver preparation injections, in order to skiagraph the dilated, kinked, or misplaced ureters; (6) for pyelography.

Skiagraphy, the Wax-tipped and Dilating Catheter. In addition to the *x*-ray, unquestionably the best and most reliable procedure in the hands of the expert skiagrapher for the diagnosis of ureteral calculus, there have been advocated a number of devices, employing the cystoscope, for the detection of stone in the ureter. The best of these is the wax-tipped ureteral catheter or bougie. If the calculus is not too large it may be released and its extrusion facilitated by the passage of the Garceau or dilating catheter and the instillation of a few cubic centimeters of sterile olive oil above and below the stone. This procedure should always be adopted before resorting to radical operation if the calculus is of small size and lodged in the pelvic or vesical portions of the ureter.

Tuberculosis. Tuberculosis of the ureter is almost invariably secondary to tuberculosis of the kidney. The ureter commonly becomes partially or completely strictured or occluded, resulting in the so-called "closed tuberculous kidney." In such cases I have twice observed the urine to be free of either pus or tubercle bacilli and the patient afebrile. Under such circumstances, catheterization of the healthy ureter, if attempted, to rule out the presence of infection of the supposedly normal side, may be done without danger of inflicting infection upon the normal kidney. On the contrary, what should be the *modus operandi*, when it is desired to ascertain the integrity of the presumably healthy kidney, when a closed tuberculosis of the other side does not exist and when the bladder obviously contains tubercle bacilli? I well recognize that some surgeons proceed to catheterize, with impunity, for purposes of urinalysis, supposedly normal ureters under these conditions. I feel that such a practice is highly condemnable, in that there is at least the theoretical possibility, by so doing, of infecting the normal ureter and kidney; furthermore, the excretion of tubercle bacilli in the urine is not a uniform process, rendering it necessary to examine twenty-four-hour specimens; hence they might not be found at the time of ureteral catheterization; and finally the demonstration of bacilli tuberculosis in the urine under these conditions does not mean necessarily surgical disease of that kidney, since the renal parenchyma will permit of the passage of tubercule bacilli as well as other bacteria without sustaining permanent disease therefrom. Indeed, it is not improbable that the catheter thus introduced may convey infection from the bladder into the ureter, and the urine per catheter thereby contain tubercle bacilli. Therefore, I believe it to be the saner and wiser

doctrine to discountenance ureteral catheterization in the presence of vesical tuberculosis until its advocates may prove the harmlessness of the procedure. In the meantime a knowledge of endovesical living pathology, particularly with reference to the character of the ureteral orifice, in conjunction with some functional kidney test, as indigocarmin, which is not dependent upon catheterization of the ureters for its performance, will suffice for the practical considerations involved in this question. Certainly, I should not permit the practice upon myself, and I have always found that the rule of self is a fine thing to apply to others.

THE KIDNEYS. The various organic and inorganic constituents of the urine must be passed over without consideration, other than to remark that both albumin and casts may be absent in nephritis, while on the other hand their presence is not necessarily indicative of primary renal disease.

Bacterin and Tuberculin Therapy. I have already alluded to the necessity of ureteral catheterization in the case of the common pyogenic infections of the kidney in order to isolate bacteriologically the etiologic organism. Thus experience has shown that certain conditions, as pyelitis, with or without cystitis, and pyonephrosis have presumably been cured with autogenous bacterins, always however, in conjunction with other well-recognized measures of merit. Again, tuberculin must be given credit for usefulness not only diagnostically, but also therapeutically in tuberculosis of the kidney. The indications for its therapeutic employment should be (1) in the earliest stage of incipiency when there is little else other than an indefinite bacilluria with both kidneys functionally sufficient; and (2) in the inoperable stage of bilateral involvement, both kidneys usually presenting insufficiency. In the latter instance I have seen it perform the incredible.

Functional Kidney Tests. The untold number of tests that have been launched from time to time to determine the functional ability of the kidneys is sufficient to prove that none has been found ideal or infallible. It is self-evident that greater reliance can be placed upon two or more tests than upon a single one. They should all be employed in conjunction with the physical, chemical, microscopic, and bacteriological examination of the urine. Those most commonly in vogue, are indigocarmin, phenolsulphonephthalein, the artificial polyuria test, the determination of urea, and cryoscopy of the blood and urine. All with the exception of the first are dependent upon synchronous bilateral ureteral catheterization for the estimation of unilateral function. Thus in the exceptional case where catheterization of the ureter is an impossibility, chromoureteroscopy with indigocarmin has rendered signal service, placing it in the foremost position as the most practical, hence the best, functional kidney test for the purpose of the surgeon. The technique of the test is extremely simple and has been detailed

by the author elsewhere. Suffice it to say that in over two hundred chromoureteroscopies I have found the test well-nigh infallible.

In deference to the phenolsulphonephthalein method it must be conceded that it is a valuable addition to modern urology, and if merely the combined kidney function is desired it may be deserving of first choice, though no more accurate than the indigocarmin test properly performed and interpreted.

Pyelography. The most important recent advance in urology has been the *x*-ray demonstration of many kidney lesions following the injection into the ureter or renal pelvis through the ureteral catheter of certain silver preparations, of which collargol in 10 per cent. solution stands foremost. Other useful preparations are silver iodide, in 5 per cent. emulsion, cargentos, and argyrol. In this manner graphic representations of the extent and character of dilatation of the ureter and renal pelvis may readily be obtained, clarifying the diagnosis of hydroureter, hydronephrosis, pyonephrosis, etc., incident to obstruction due to bladder retention and ascending infection, extra-ureteral pressure, stricture, and calculus. The characteristic bizarre figures of the distorted pelvis occasioned by the irregular growth of kidney tumors is easily recognizable. Congenital malformations, as fused or horseshoe, solitary, supernumerary, and pelvic kidneys, anomalous ureters and movable kidneys, with twisted or angulated ureters, can best and often only be demonstrated clinically by skiagraphic injections.

Syphilis. No disease to which man falls heir has been so thoroughly, effectively, and profitably studied in the past decade as syphilis. The years 1905, 1906, and 1909, representing respectively the discovery of the cause, the most important aid in diagnosis, and a valuable addition to the treatment of the disease, form a triad never to be forgotten in the annals of syphilology. Today the inflexible rule never to start the treatment of syphilis until the diagnosis is surely established, remains just as imperative as in the past; but we are invariably in a position to formulate that diagnosis much earlier, and there is little excuse to await the secondaries for diagnostic purposes. Nor are we obliged to depend upon the Wassermann reaction in the primary stage, since this may be negative even in the absence of treatment until the fifth week. Although the fixation of the complement test is undoubtedly the most useful and reliable means for determining the presence of syphilis, we have, especially in the primary stage, when serum diagnosis may avail naught, other procedures permitting of the correct judgment of the lesion in the first day or two, at the time when intensive modern treatment apparently may effect a speedy cure.

The Dark Field Illuminator. By virtue of the construction of this apparatus, consisting of a microscope fitted with a special

substage reflector, whereby the rays from a powerful source of light are brought to a focal point 1 mm. above the ground illuminator, any solid body, as the Treponema pallidum, intercepting these rays at their focal point, will appear luminous; all else is invisible, and forms a dark or black ground. The principle is precisely that observed when a beam of light penetrates a hole and illuminates the dust in a dark room. With this device the discovery of the Treponema pallidum in the early chancre, often long before the serum reaction becomes positive, is a comparatively simple act, and seldom fails to disclose the causative organism in the primary lesion of syphilis. Success depends upon the proper preparation of the specimen, and consists largely in the preliminary cleansing of the sore with warm water, followed by firm pressure to obtain a free exudation of lymph or serum containing as few red blood cells as possible. So constant are the findings by this method, and so important is it to establish the diagnosis, early in view of the most successful treatment, that I consider the dark ground illuminator an indispensable addition to the diagnostic armamentarium of each syphilographer for the proper and best handling of his cases.

The Stained Smear. A less reliable method for the demonstration of the Treponema pallidum is the stained smear. Many good stains have been suggested for this purpose, but there is one to which I especially desire to direct your attention. It is that by the eosin-azur method, previously described in this paper in connection with the diagnosis of gonorrheal urethritis. The stain possesses differential properties, the treponemas appearing faintly purplish. I know of no stain which so ably fulfils the requirements both for gonococcus and treponema. In doubtful primary sores, if the dark field illuminator be not at hand an attempt, repeated if necessary, should always be made by this method to demonstrate the treponema. Caution must be exercised in the preparation of the smear and the differentiation of the Treponema pallidum from the microdentium, pertenuis, and Spirochæta refringens is imperative.

Levaditi's Tissue Stain. By recourse either to smear or tissue-stained preparations the Treponema pallidum has been demonstrated in every lesion of syphilis. The best method for histopathologic demonstration is Levaditi's modification of the Ramón y Cajal silver-nitrate stain. This procedure has been largely superseded by the serum test of Wassermann, hence its technique will not be described.

Noguchi's Luetin Test. Noguchi is the first investigator to have succeeded, unquestionably, in growing in pure culture the Treponema pallidum. Thus he was enabled to accomplish what many others had attempted—namely, an allergic response in syphilitics analogous to the von Pirquet specific cutaneous tuberculin test

as applied to tuberculosis. His luetin is a fluid preparation made by grinding in a mortar the ascitic fluid agar and the ascitic fluid growths, cultivated anaërobically in the presence of pieces of placental tissue. This is sterilized, as is customarily the case, in the preparation of bacterins and standardized by the dark field microscope.

After sterilization of the skin of both arms at the sites selected for the inoculations, one arm is injected intradermically, using a fine needle, with 0.05 c.c. of luetin in two places; the opposite arm is injected with a control emulsion. Normal or negative reactions commence to recede always within seventy-two hours. Positive reactions may assume one of three forms, the papular, the pustular, or the latent. They make their appearance in twenty-four to forty-eight hours up to the fourth or fifth day, and in the latent form may light up even after the tenth day. In an analysis of 400 cases, Noguchi has found that the luetin test is not as reliable as the complement-fixation test in the primary, secondary, and parasyphilitic stages; he found it most servicable in the tertiary and hereditary manifestations of the disease, being positive in 100 per cent. of manifest tertiary affection and 96 per cent. of hereditary syphilis. The test should certainly prove of great value, particularly when improvements in the preparation and potency of the luetin are possible, to those practitioners not being in a position or not caring to employ the Wassermann reaction.

The Butyric Acid Test. This method, suggested by Noguchi for the detection of the active lipotropic syphilitic antibodies in the cerebrospinal fluid and blood serum, depends upon the precipitation of globulin on the addition of butyric acid. The application of the test varies somewhat whether the spinal fluid or blood serum is employed. Noguchi himself seems not particularly impressed with the blood application of the test, but claims in certain neurologic syphilitic manifestations that it supersedes in reliability and value the Wassermann reaction. This assertion has not been accorded universal confirmation where the most approved technique for the complement-fixation test has been employed. Nevertheless the reaction occurs quite regularly in the cerebrospinal fluids of patients with syphilitic and parasyphilitic affections, and runs a parallelism with the cytodiagnosis of parasyphilitic disease. In addition to syphilis the reaction occurs in many of the other diseases involving the central nervous system, as influenza, pneumonia, tuberculosis, cerebrospinal meningitis, anterior poliomyelitis, etc., but these conditions are usually readily differentiated or excluded. The test is unquestionably of great value, and irrespective of its relative comparison with the Wassermann reaction, because of its simplicity can be carried out in any laboratory.

The Wassermann Reaction. Time and desire at present exclude a detailed consideration of the technique of the complement-

fixation test for syphilis. The most brilliant modification of the Wassermann reaction is that by Noguchi. Theoretically, employing the most approved technique, Noguchi's method would have more to recommend it if it were more simple in its performance than the Wassermann. Noguchi's contention that his method is more delicate in the detection of the syphilitic antibody than the Wassermann technique, the inaccuracy of which depends upon an unknown amount of natural hemolytic amboceptor in the patient's serum against sheep's red blood corpuscles, has not been confirmed in the experience of those employing the best Wassermann technique, wherein a standardized complement unit, a properly titered hemolytic amboceptor, together with careful standardization of red blood corpuscles and antigen are used.

That the complement-fixation test of Wassermann is the most valuable and reliable diagnostic aid for syphilis in general is no longer disputable. Positive reactions, with the following exceptions, which can almost invariably be excluded in other ways, mean syphilis. The exceptions are in yaws, relapsing fever, trypanosomiasis, tubercular leprosy, certain drug narcoses, as from morphin, scopolamin, veronal, and ether, and in sera obtained just before or after death. It is plausible to think that when in the performance of the reaction, specific antigen of a pure culture of Spirochætæ pallida instead of the customary lipotropic substances can be employed the exceptions may be rendered fewer.[2]

A negative reaction, on the other hand, does not mean necessarily that syphilitic infection is absent. Treatment, whether by mercury or Ehrlich's arsenical preparations, may prohibit the occurrence of a positive reaction for a few days to many months. This of course depends upon the virulence of the infection on one hand and upon the intensity of the treatment on the other. I have repeatedly observed after a moderate mercurial administration a negative reaction for several days, which after two or three weeks became positive. On the contrary in the latent stage of the disease, when the serum may exhibit a negative Wassermann reaction, a provocative positive reaction may be elicited by multiple injections of mercury or by the administration of 0.02 to 0.05 gram of salvarsan or neosalvarsan. However in the absence of any treatment following the appearance of chancre I have never seen a case in which a negative reaction persisted for a longer period than four weeks. In the event of insufficient treatment I have seen many reactions continuously negative for six to nine months after the cessation of treatment once more become positive. In view of this, and the fact that approximately one-third of all patients who have passed through the classic mercury and

[2] Since this article was written and read, investigations along this line by Dr. John A. Kolmer have shown, however, that such is not the case.

iodine form of treatment, even in the absence of symptoms, still give the complement-fixation test, evidencing their proclivity to parasyphilitic lesions, as paresis, locomotor ataxia, etc., we have come to regard the Wassermann reaction employing the standardized single complement-unit as originally suggested by Laird, not the multiple complement-unit system as more important for the control of treatment than for the diagnosis of the disease. Thus as a tentative plan no patient should be discharged cured until he presents for a period of at least two years after discontinuance of treatment a continuously negative Wassermann taken at three-month intervals. Even at the expiration of that time the safest procedure is to repeat the test yearly indefinitely.

I would state that the Wassermann reaction, with proper technique and precautions, has been found as indispensable in syphilology as it is well-nigh infallible.

Salvarsan and Neosalvarsan. The indication for these remedies is popular knowledge. The technique of their preparation for and mode of administration is indifferently and carelessly observed, and I have known fatalities to occur not on account of the drugs themselves but because of the heedlessness or incompetence of the physician. Therefore in the belief that Ehrlich is more familiar with the chemical and potential harmful properties of these synthetic preparations than we are, I think it behooves us to follow strictly his advices in the administration of the drug. Thus he advises in the case of neosalvarsan that the drug should be dissolved in a solution at 68° to 72°, and administered to the patient at that temperature, that it should not be shaken unduly and should be given immediately, because of its unstable characteristic. Although "914" is acknowledged to be not nearly so toxic as "606," two deaths even from neosalvarsan have been reported from Europe.

It is too early to pass judgment finally upon the relative merits of salvarsan and neosalvarsan, but from an experience of several hundred injections I feel convinced that the latter is not so immediately effective as the former preparation at least in the secondary period of syphilis. In practically all stages of the disease, excepting the parasyphilitic manifestations after degeneration of nervous tissue has supervened, we know that these arsenic preparations suffice to produce symptomatic cure, either in single or multiple dosage; respecting their ultimate or permanent curative effect, we know absolutely nothing. A few years must elapse before conclusions can be drawn. At present the treatment of syphilis is truly empiric, although with the promise that we possess in Ehrlich's preparations remedies of paramount importance, capable of shortening very materially the required period of treatment.

Approximately 10 to 20 per cent. of patients studied to date have apparently been cured by single or multiple injections of

salvarsan and neosalvarsan alone, judged by the non-appearance of secondaries and a continuously negative Wassermann for a period of two years. Almost all these have been patients who received the drug during the first week of the chancre. Experience has also shown that with the exception of the first few days of the disease multiple doses, unless contraindications arise, should be administered. Moreover, both from the Wassermann reaction control as well as from the clinical symptomatology, it is obvious that the treatment must be intensive from the start, and that to be most effective the arsenic should precede the mercury. Consequently we have adopted the tentative procedure in all stages of the disease, with the exception of the earliest primary, to administer salvarsan or neosalvarsan, always intravenously, in multiple doses, usually three, at intervals of a week or two unless contraindications exist. Coincidently the patient is placed on a vigorous campaign of mercury—or if in the tertiary stage, mixed treatment—for six months or a year. On suspension of the mercurial or mixed treatment he is again given one or more injections of salvarsan or neosalvarsan. Thereafter the renewal of treatment or the pronouncement of cure is governed by periodical determinations of the Wassermann reaction.

AN ORTHODIAGRAPHIC STUDY OF A CASE OF BRONCHIAL ASTHMA.

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Fluoroscopic examinations of patients with bronchial asthma have been described by Krause,[1] Dally,[2] Jamin,[3] Levy-Dorn,[4] Schlesinger,[5] and others. These have shown a diminished density of the pulmonary tissue, a horizontal position of the ribs, widening of the intercostal spaces, a low, flattened diaphragm, and a heart low and in the median line. The orthodiagraph enables us to

[1] Atlas und Grundriss der Röntgendiagnostik, edited by Franz M. Groedel, München, 1909, pp. 70 to 71.

[2] On the Use of the Röntgen Rays in the Diagnosis of Pulmonary Diseases, Lancet, June, 1903, xxvii, 1800 to 1806.

[3] Atlas und Grundriss der Röntgendiagnostik, edited by Franz M. Groedel, München, 1909, pp. 56 to 57.

[4] Ein Asthmatischer Anfall im Röntgenbilde, Berlin. klin. Woch., 1896, xxxiii, 1046 to 1048.

[5] Zur Lehre vom Asthma Bronchiale, Wien. klin. Woch., 1898, xi, 265 to 366.

record these changes accurately from day to day. The following case was studied by this method for a period of eight weeks, and is of particular interest in that it shows the slow return to normal after complete cessation of a prolonged attack of asthma.

Mrs. S., aged twenty-seven years, entered the University Hospital on January 29, 1912, suffering from bronchial asthma. Her attacks of asthma began at the age of nine years. After a brief period of relief about the time of puberty these attacks reappeared at the age of fifteen. She was married at seventeen and remained practically well until twenty years of age. During this interim three children were born, but after the birth of the last child the attacks recurred. Since 1907 the attacks have become more severe and have frequently lasted for weeks at a time, leaving the patient in a weakened condition. All the customary remedies have been tried, but none have proved reliable in preventing or aborting her attacks.

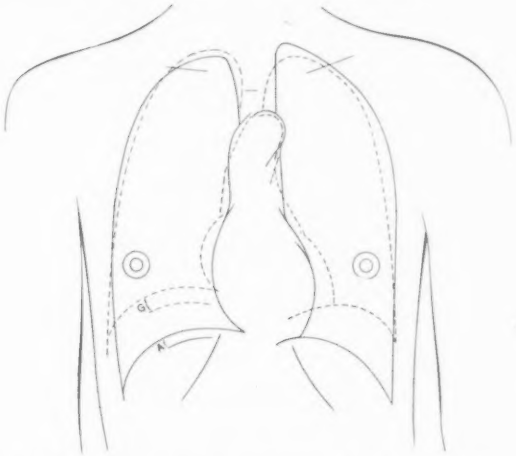
The patient entered the hospital toward the end of a prolonged attack of asthma, which had confined her to bed for four months. She had been receiving, hypodermically, as much as a grain and a half of morphin a day, for this seemed to be the only method of relieving her severe dyspnea.

Examination showed moderate emaciation. She was markedly dyspneic and the accessory respiratory muscles were used constantly. The anteroposterior diameter of the thorax was increased and the borders of pulmonary resonance unusually low. Costosternal joints moved freely. No rales were heard over the thorax on the day following her admission and none thereafter during her stay in the hospital. Almost immediately after coming into the hospital the severe symptoms abated without the use of any medicine. The morphin was withdrawn and the patient's general condition gradually improved. She was discharged March 23, 1912, in good condition, save for slight dyspnea on exertion.

One month later she returned to the hospital, shortly after the onset of a fresh attack of asthma. On this occasion numerous musical rales were heard over all parts of the chest; this attack also subsided while in the hospital. At no time did the blood show an eosinophilia or the sputum Curschmann spirals. Aside from these, however, the patient seemed to have had a typical bronchial asthma.

An orthodiagraphic examination made the day following the first admission showed an extreme degree of pulmonary distention, with a low and flat diaphragm and the heart in the vertical position (see diagram). It is well known that pulmonary distention accompanies bronchial asthma, but its exact extent and its duration after the attack has never, to our knowledge, been accurately determined by means of the orthodiagraph. The impression seems to prevail that the acute pulmonary distention of asthma

usually disappears promptly after the attack, although Jamin states that a less marked distention may possibly remain for some



Continuous line shows position of diaphragm, heart and lung borders at entrance. *A* indicates diaphragm excursion at height of distention. Dotted line shows position of same organs at discharge. Note diaphragm excursion (*G*) at this time.

indefinite time. Our patient continued to show a diminishing lung volume over a period of seven weeks. The gradual changes are shown in the following chart.

TABLE I.

Date.	Area[6] of right lung.	Area of left lung.	Total lung area.
January 29, 1912	185.5 sq. cm.	173 sq. cm.	385.5 sq. cm.
February 8, 1912	167.0 sq. cm.	163 sq. cm.	330.0 sq. cm.
February 12, 1912	158.0 sq. cm.	165 sq. cm.	323.0 sq. cm.
February 16, 1912	152.0 sq. cm.	158 sq. cm.	310.0 sq. cm.
February 27, 1912	148.0 sq. cm.	156 sq. cm.	304.0 sq. cm.
March 5, 1912	143.0 sq. cm.	145 sq. cm.	288.0 sq. cm.
March 9, 1912	142.0 sq. cm.	152 sq. cm.	294.0 sq. cm.
March 16, 1912	146.0 sq. cm.	146 sq. cm.	292.0 sq. cm.
March 21, 1912	137.0 sq. cm.	132 sq. cm.	269.0 sq. cm.

On the second admission the following areas were found as the condition improved.

TABLE II.

Date.	Area of right lung.	Area of left lung.	Total lung area.
April 22, 1912	174.0 sq. cm.	173.5 sq. cm.	347.5 sq. cm.
April 26, 1912	178.6 sq. cm.	183.5 sq. cm.	362.1 sq. cm.
May 6, 1912	157.2 sq. cm.	139.0 sq. cm.	296.2 sq. cm.
May 8, 1912[7]	147.5 sq. cm.	146.0 sq. cm.	293.5 sq. cm.

[6] These areas were measured by the planimeter on orthodiagraphs taken in the usual antero-posterior directions.

[7] At this date the patient left the hospital, although her lung area had not reached the lowest point seen on the previous admission.

This gradual subsidence of the pulmonary distention derives particular interest from its possible relation to permanent pulmonary distention in chronic emphysema. Acute distention of the lungs, such as occurs during exercise, is known to pass off almost immediately (Bohr[8]) or to last at most only a day or two (Durig[9]). The effect of repeated and prolonged distention, such as may occur in severe bronchial asthma or in chronic bronchitis, is less well understood. It is commonly held by clinicians that these may lead to permanent pulmonary overdistention, even after the exciting causes have disappeared; yet the proof of this by objective methods has not been furnished and other theories have been advocated to account for chronic pulmonary overdistention. So far as our patient is concerned the obstructions in the bronchi, as judged by an absence of rales, cleared up shortly after she first entered the hospital, and it seems to us that the slow return to a normal lung volume can best be explained on the assumption of a partial loss of pulmonary elasticity with slow recovery. Our observations therefore favor the view that a severe and continued overdistention of the lungs, due to obstruction in the bronchioles, may exert a prolonged effect on the pulmonary volume even after the cause has disappeared; and it seems probable that if attacks of asthma continue, or if the lungs are damaged by disease or by age, a permanent distention might result from this cause.

While it is generally agreed that the diaphragm is low during the attacks of asthma, there have been differences of opinion regarding its movements. Levy-Dorn first described a unilateral immobility of the diaphragm during an attack of asthma. While viewing the patient a fit of coughing terminated the attack and the diaphragm then began to move. He ascribed this immobility to the pressure of the greatly inflated lung and not to a spasm of the diaphragm. Dally has observed the same phenomena. Jamin observed that the motion of the diaphragm was greatly diminished in comparison with the strong respiratory movements of the thorax. He noted that the diaphragm moved downward slowly on inspiration and returned much more slowly to its position during expiration. Krause observed nine cases, in four of which he noted an immobility of one-half of the diaphragm, three times on the right and once on the left side. The other half of the diaphragm made short, quick, jerky movements with an excursion much less than the normal. He believed that there was a unilateral spasm of this muscle. As the condition returned to normal the spasm gradually lessened and the movement of the two halves of the diaphragm became equal and uniform. In five other cases he noted jerky

[8] Die Funktionellen Aenderungen in der Mittellage und Vitalkapazitaet der Lungen, Arch. f. klin. Med., 1907, lxxxv, 385.

[9] Ueber die Groesse der Residualluft, Centralb. f. Phy., 1903, xvii, 258 to 267.

movements of the diaphragm, with small excursion of both halves. Both sides were distinctly mobile. On the first examination our patient showed slight movements of the diaphragm on both sides, but the extent of the movements (as seen in the diagram) was much less than normal. As the pulmonary distention disappeared the diaphragmatic movements gradually increased and reached their maximum at the end of her stay in the hospital. At this time the diaphragm stand was 3 cm. higher than its position at the beginning of the attack, and the respiratory excursion had increased from 0.5 cm. to 1.5 cm. On the second admission, during an attack, there was no spasm of the diaphragm observed, but the right side moved slightly upward during inspiration and downward during expiration. We are inclined to explain these paradoxical movements as due to a relatively motionless diaphragm, which was carried up and down by the excessive thoracic movements.

As described by Levy-Dorn the heart in asthma is low with the apex in the sixth interspace near the sternum, the right border reaching considerably beyond the sternum. Moritz showed a diminution in the size of the heart in one case, and Goetzl and Kienboch[10] observed the same during an attack in two cases. Dietlen[11] reports six cases in which the heart shadow was determined during an attack in both inspiration and expiration. He observed that the heart silhouette was smaller during expiration than during inspiration, which is the reverse of that usually found in normal man, and he explained this as due to the increase of intrathoracic pressure during expiration, which obstructed the venous inflow and possibly compressed the heart. The heart of our patient on entrance was in the vertical position (Fig. 1), and it showed a surface area of 64 sq. cm. As the pulmonary distention lessened the heart became less vertical, and although its shape varied somewhat from time to time the surface area remained almost constant.

TABLE III.

Date.	M. R.	M. L.	Total width.	Area of heart.
January 29, 1912	2.5 cm.	5.5 cm.	8.0 cm.	64 sq. cm.
February 8, 1912	3.0 cm.	5.4 cm.	8.4 cm.	60 sq. cm.
February 12, 1912	3.9 cm.	5.5 cm.	9.4 cm.	66 sq. cm.
February 16, 1912	2.9 cm.	7.6 cm.	10.5 cm.	67 sq. cm.
February 27, 1912	3.9 cm.	5.7 cm.	9.6 cm.	67 sq. cm.
March 5, 1912	4.1 cm.	5.7 cm.	9.8 cm.	61 sq. cm.
March 9, 1912	4.0 cm.	5.4 cm.	9.4 cm.	63 sq. cm.
March 16, 1912	4.3 cm.	5.2 cm.	9.5 cm.	61 sq. cm.
March 21, 1912	4.1 cm.	5.7 cm.	9.8 cm.	62 sq. cm.

[10] Asthma bronchiale und Verkleinerung des Herzens, Wien, klin. Woch., 1908, xxi, 1261 to 1265.

[11] Orthodiagraphische Untersuchungen über pathologische Herzformen und das Verhalten des Herzens bei Emphysema und Asthma, Münch. med. Woch., 1908, lv, 1770 to 1773.

CONCLUSIONS. In a patient with severe and repeated attacks of asthma the pulmonary distention continued for several weeks after a cessation of a prolonged attack. This distention caused the heart to assume a vertical position, but did not influence its surface area. During the attack of asthma the diaphragm moved but slightly, and movements in reverse of the normal were observed. In explaining such reversed movements, however, one must take into account the excessive thoracic movements which act on the diaphragmatic attachments. The movements of these attachments may more than neutralize the movements due to the diaphragmatic contractions, so that the crests of the diaphragm may seem to execute reversed movements.

A CONTRIBUTION TO THE STUDY OF HEREDITARY DEGENERATION (PSEUDOHYPERTROPHIC MUSCULAR DYSTROPHY IN COMBINATION WITH DEGENERATION IN THE CENTRAL NERVOUS SYSTEM).

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WHEN only certain parts of the nervous system are congenitally defective they are likely to be those having close functional relations to each other, and in consequence there develop in such cases certain functional disturbances which enable the nature and location of the anatomic lesion to be diagnosticated with accuracy. It is well known also that these defects may not be apparent until the individual has attained a certain age, when, seemingly from the mere stress of living, the defective parts undergo retrogressive changes, and symptoms of disability appear, the nature of which depends upon the functions of the part affected. In these cases of so-called abiotrophy a strong reason for believing that the anatomic change and the resulting clinical phenomena are congenital in origin is their tendency to become a characteristic of certain families.

The literature of these family degenerative conditions is quite extensive, but for the most part the published studies on the subject may be divided into those which deal with the localization and character of the histopathologic changes in the nervous system or other tissues involved and those concerned with attempts to classify them into types according to the symptoms presented or the parts affected, which are then considered as separate and

distinct diseases. A study of the literature leads to the conclusion that there are in all these cases histopathologic changes of a degenerative character in the various tissues, and that the clinical types depend largely, if not solely, on the location of the lesion. From this it follows that if there was present in the parental organism a toxic substance or disease capable of causing degenerative changes in the nervous system or elsewhere, and this toxic substance or disease could be transmitted to offspring, those offspring might show similar degenerative changes. Under such circumstances we would be dealing not with an hereditary degeneration but with a degeneration due to disease or toxemia possibly preventable or treatable. The question arises whether we have any way of differentiating a truly hereditary chracteristic from an acquired degenerative condition caused by a neurotoxin transmitted from parent to child.

These dystrophies, when they affect the nervous system, give rise to various fairly definite symptom-complexes, such as Friedreich's ataxia, family spastic paraplegia, etc. The muscular dystrophies are also divided into various types: the pseudohypertrophic form of Duchenne; the juvenile form described by Erb; Leyden's form; the facioscapulohumeral type (Landouzy-Dejerine); Zimmerlin type, beginning in the thorax muscles and affecting the upper extremities before the lower; a type described by Jendrassik as congenital, that is, the manifestations begin at birth; and the Werdnig-Hoffman type, beginning in infancy and affecting several members of the same family, but so frequently these types are combined with each other or present anomalous characteristics that we have the authority of Erb[1] that their differentiation is a matter of great difficulty. They are usually familial, and are regarded as quite distinct from the spinal type of progressive muscular atrophy; and from the neural, or Charcot-Marie-Tooth type, variations of which are described by Gombault, Dejerine-Scottas, Eichorst, Brossard, and others. It is certain, however, that progressive spinal muscular atrophy may be hereditary, as in the case reported by A. Strümpell[2] and in a similar case reported by Bernhardt.[3] If such is the fact we have an instance of a condition usually regarded as due to some unknown, acquired cause becoming hereditary. There are two possible explanations: one is that an acquired degeneration has become hereditary, which is opposed to Weismann's theory of heredity; or that the cause of the degeneration in the parent was transmitted to the offspring and became in turn the cause of the degeneration there. The observations of William G. Spiller[4] that syphilis might be a cause

[1] Deutsch. med. Woch., 1910, S. 1865.
[2] Deutsch. Zeitschr. f. Nervenheilk., 1893, Band iii, S. 471.
[3] Virchow's Archiv, Band cxv, Heft 2, S. 197.
[4] Jour. Nerv. and Ment. Dis., 1912, p. 584.

of the so-called primary lateral scleroses and of progressive spinal muscular atrophy, and the case recorded by S. Leopold[5] of progressive spinal muscular atrophy, in which necropsy showed some evidence of syphilis, suggests at least one such cause that can be acquired and can also be transmitted to the offspring.

As bearing on this question, I wish to record a case observed by me in which a parent and probably also a grandparent had the spinal type of progressive muscular atrophy, while the patient presented the classical picture of the pseudohypertrophic form of muscular dystrophy. The occurrence of such a case indicates a close relationship between these two conditions.

John C., aged three years, was admitted to the Hospital of the University of Michigan November 20, 1909. His mother was well. His father could not be examined, but, according to the description furnished, was suffering from a disability which began with wasting of the small muscles of both hands, producing a clawhand, and this wasting had extended up both arms to the shoulders. The affection was painless and not accompanied by any change in the sensibility of the hands, and there was no involvement of the lower extremities. It may be inferred that he was suffering from the progressive muscular atrophy of the spinal type. Chronic anterior poliomyelitis may be ruled out by the statement that the atrophy was quite pronounced before any marked weakness was noticed. There was also a statement that the patient's grandfather on the father's side had an affection similar to the father's, but an accurate description of his condition was unobtainable. The mother of the patient had had one miscarriage before he was born, and the patient had a younger brother apparently well.

The patient was born at full term, with instruments, and was seemingly normal and uninjured. He learned to talk at the age of ten months and to walk at one year. He had measles in the summer before his admission to the hospital, and a light attack of pneumonia at the same time. His present trouble apparently began when he was about the age of two years, when some difficulty in walking was noticed, and this became progressively worse until his admission to the hospital. An examination at that time showed a child of about normal size for his age, hair light and fine, a well-nourished appearance, intelligent expression, and a well-shaped head. He understood and obeyed commands, answered questions readily, and appeared to have a normal mentality. The pupils were equal, reacted to light and in accommodation, and there were no extraocular palsies. The ocular fundi appeared normal. There was no paralysis of the face or tongue. The arms, forearms, and shoulders were rather thin, but all movements were normal, and there was no fibrillary tremor. There was no atrophy of the small

[5] Jour. Nerv. and Ment. Dis., 1912, p. 606.

muscles of the hands. When standing there was a marked lumbar lordosis and protrusion of the abdomen; this was present also when sitting or lying on his side; it disappeared when lying on his back. There was no lateral curvature of the spine. The thighs appeared to be about the normal size, but the calves of both legs were distinctly larger than normal, and felt very firm. There was no paralysis or deformity of the legs or feet and he could walk without support, but has a waddling, typically dystrophic gait. In arising from a prone position he turned over and rose on his hands and knees. He then attempted to rise to a standing position by pushing with his arms, but was apparently too weak to so do without assistance. The biceps-jerks were present on both sides, but the knee-jerks and Achilles-jerks were not obtained. No sensory loss could be detected anywhere. The skin reflexes were all present. Plantar irritation caused flexion of the toes.

While the age of the patient suggests the Werdnig-Hoffman type of muscular dystrophy, a pseudohypertrophy such as was present here rules out that diagnosis according to Hoffman.[6] We have then an instance of progressive spinal muscular atrophy in the father and grandfather and pseudohypertrophic muscular dystrophy in the child. I have not been able to find a similar case of heredity in the literature, but K. Mendel[7] reported a case in which the symptoms of progressive spinal muscular atrophy were combined with those of a pseudohypertrophic muscular dystrophy in a boy, aged sixteen years. The condition was not hereditary.

Eulenberg and Cohn,[8] under the title of "family dystrophic heredodegeneration," reported four members of the same family, aged from eight to sixteen years, affected with a progressive muscular atrophy beginning in the face and upper extremities and accompanied by pseudohypertrophy of the calves and lost knee-jerks, but they regarded these cases as a peculiar type of muscular dystrophy rather than as a combination of types.

While the dystrophies are usually hereditary, and thereby differ from the progressive spinal muscular atrophies which are not, usually, there are many cases of muscular dystrophy in which no hereditary influence can be detected. I have seen a boy, aged twelve years, suffering from a typical muscular dystrophy of the pseudohypertrophic type, but the most careful inquiries failed to show any trace of hereditary degeneration. The parents were healthy and not blood relations. They had two other children, one older and one younger than the patient, who were normal. All of the grandparents and the aunts and uncles of the patient were living, and showed no apparent abnormality. The patient

[6] Deut. Zeitschr. f. Nervenheilk., 1893, S. 427; ibid., 1897, S. 292; ibid., 1898, S. 418.
[7] Neurolog. Centralbl., 1901, S. 601.
[8] Ibid., 1911, S. 963.

presented typical signs and symptoms of the disease, which it would be unnecessary to record in detail.

It is not uncommon to find atypical cases of muscular dystrophy or combinations of two or more types in the same patient, as Erb has pointed out. It is, however, much less common to find the combination of a muscular dystrophy with the spinal heredodegenerations. Such cases do occur, however, and are of considerable clinical importance, primarily because of the liability to errors in diagnosis.

The following case is an instance of the combination of Friedreich's ataxia with a pseudohypertrophic muscular dystrophy in the same patient:

Carl K., aged ten years, was admitted to the Hospital of the University of Michigan July 24, 1912. On his admission the following history was obtained from his parents:

His father and mother were living and well, and the patient had two sisters, one five years old and one seven, both in good health. There were no nervous disorders on the father's side of the family but the mother said that she had two brothers; the older one was well, but the younger one had an affection similar to the patient's, coming on at the age of ten and causing his death at the age of eighteen years. Her father and his brothers were free of any nervous disorder, but her mother's brother had a similar complaint, beginning at ten and fatal at eighteen years.

The patient was a first child, and was delivered with instruments, but apparently not hurt. He was bottle-fed, and had diarrhea in his first year. He walked and talked at about the usual age, and appeared to be a normal child. Measles and whooping cough were the only infectious diseases he had, and there was no history of injury. He had never had any convulsions.

At an early age, about four years, it was noticed that he had some difficulty in walking—a waddling gait—and this difficulty slowly increased; but about one year before his admission to the hospital his gait became much worse, and it was noticed that he walked on his toes. About June 1, 1912, he became unable to walk at all. He had severe headaches for about a year, usually coming two or three times a week, and his father stated that his school work was poor for this year; he seemed to have difficulty in learning, and also was forgetful. He had no other symptoms.

On examination, July 26, 1912, it was noted that he seemed to be a well-nourished, intelligent boy, with few stigmas of deviation and no stigmas of hereditary syphilis.

The pupils were equal, and reacted to light and in accommodation. There was a distinct nystagmus on lateral deviation of the eyeballs. There was no paralysis or atrophy of the face or tongue. There was no disturbance in speech or deglutition. The grip of both hands was weak, especially the left. He could raise both

arms above his head, but his power to resist passive movement of the elbows and shoulders was less than normal. There was no atrophy or deformity of the hands, arms, or shoulders, no fibrillary tremor and no ataxia in the finger to nose test, with the eyes open or closed. The biceps-jerks and triceps-jerks were not obtained on either side. The patient sat in his wheel chair leaning forward on his elbows. He could not walk and could stand only if all his weight was supported from his shoulders. He stood on his toes. The thighs and buttocks were normally developed for his age, but the calves of both legs were abnormally large and felt firm on pres-

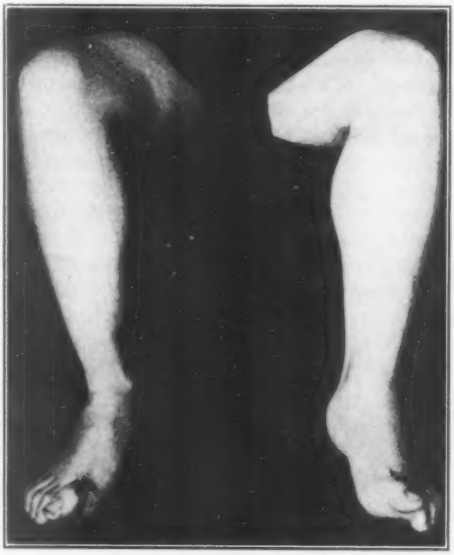

FIG. 1.—Pseudohypertrophic muscular dystrophy and Friedreich's ataxia, showing the 'Friedreich foot.'' The foot is shortened, and there is permanent hyperextension of the proximal phalanx and flexion of the terminal phalanx of the great toe. Note also the pseudohypertrophy of the calf muscles.

sure. There was a distinct talipes equinus in both feet, with hyperextension of the first phalangeal joint of the great toes and flexion of the terminal joint (Fig. 1). There was no atrophy of the small muscles of the feet. All normal movements of the legs and feet were possible but weak. The knee-jerks were present on both sides, but were diminished. The Achilles-jerks were present on both sides. Plantar irritation caused extension of the great toe on each side. The cremasteric and abdominal reflexes were present on both sides. Tactile sensation was normal on the face, body, and extremities, and the localization of sensation was normal on

the legs and feet. There was no analgesia or thermasthesia, and no loss of the sense of motion or position in the fingers or toes. A general physical examination was negative. The urine examination showed a specific gravity of 1020; no albumin; no glucose; no bile; urea, normal amount; sediment was normal. An examination in the opthalmologic clinic, by Dr. Walter Parker, showed: nystagmus on lateral deviation of the eyeball; pupils equal; reflexes normal; no gross lesion.

July 29. Began taking *x*-ray treatments to the spine three times a week. A "soft tube" was used and the distance about 12 inches. Ten minutes exposure was given the entire spine.

July 31. Blood count showed: red blood cells, 4,500,000; leukocytes, 10,000; hemoglobin, 85 per cent.

He was re-examined in August and September, with practically the same findings. The headaches entirely disappeared after the first week of *x*-ray treatments, and he was able to stand by grasping a small topped table and resting his chest against it. In standing this way his back was bent forward and his legs widely separated; if the buttocks were supported he showed a marked lumbar lordosis. Irritation of the soles of the feet produced extension of the toes on each side and also a movement of withdrawal of the entire leg ("reaction of defence," Babinski). A general physical examination showed nothing pathologic in the viscera, no glandular enlargement, and a normal development of the external genitalia. A Wassermann reaction on the blood was negative, and examination of the cerebrospinal fluid showed no abnormal chemical or cellular constituents.

Cases of Friedreich's ataxia and muscular dystrophy have been reported by Jendrassik,[9] with an anatomic study by Kollaritis.[10] Cases are also reported by Baumlin[11] and Bing.[12] A similar case but without any family history of either disease is reported by Jastrowitz.[13] Cases of muscular dystrophy, such as the one reported by O. Crouzon,[14] in which there was present a positive Babinski sign, and that of H. Schlesinger,[15] in which the patient developed a pes equino valgus in both feet early in the disease, are cases somewhat resembling these. Greenfield[16] reported a case of Friedreich's disease combined with the peroneal type of progressive muscular atrophy. Cases of spastic spinal paralysis, nystagmus, and tremor are reported Jendrassik,[17] who refers to similar cases

[9] Deutsch. Zeitschr. f. Nervenheilk., 1902, S. 444.
[10] Deutsch. Archiv f. klin. Med., 1901, Band lxx, S. 157.
[11] Deutsch. Zeitschr. f. Nervenheilk., 1901, S. 265.
[12] Deutsch. Archiv. f. klin. Med., 1905, S. 199.
[13] Neurolog. Centralbl., 1911, S. 426.
[14] Revue Neurologique, 1912, p. 109.
[15] Neurolog. Centralbl., 1901, S. 143.
[16] Proc. Royal Soc. Med., London, v, No. 3, Neurol. Sec., p. 75.
[17] Deutsch. Archiv. f. klin. Med., 1897, Band lviii, S. 137.

reported by Maas, Seeligmüller, and Hoffman. These cases probably represent still another combination of heredodegenerative conditions.

A case of pseudohypertrophic muscular dystrophy combined with optic neuritis is not mentioned by Jendrassik[18] in his collection of transitional and combination types of heredodegenerations. Such a case was admitted to my service at the Hospital of the University of Michigan May 27, 1912:

Floyd B., aged eight years, complained chiefly of difficulty in walking. No history of the case was obtainable except from the patient himself, who said that his mother was dead and that his father had deserted the family. He said that he had three brothers, and they all had trouble similar to his. He did not remember that he ever had any serious illness, but said that he never went to school and that he could not read or write. An examination on his admission to the hospital showed a pleasant, well-mannered child, who obeyed all simple commands, dressed and undressed himself, untied knots normally, and was about the average size for a child of nine years. His head was of normal shape, his ears rather prominent, and Darwin tubercles were present on both ears. The pupils were equal, reacted to light and in accommodation. The extraocular movements were normal. There was no facial palsy. The tongue protruded straight, and there was no tremor or atrophy of the tongue. The masseters and temporals contracted well and equally. He had no difficulty in moving his head. There was no tremor of the hands on extension. There was no disturbance of the gross movements of the arms, and there was no incoördination of the hands in the finger to nose test. The muscular strength in the arms in flexion and extension was equal and good in both arms. There was no atrophy or deformity of the arms or hands and no fibrillary tremors were noticed. The grip was equal and good in both hands. The patient walked with a broad base, but there was no ataxia and no apparent spasticity in the legs. His station was equally as good with his eyes open as with them closed. There was marked weakness in extension of the legs and dorsoflexion of the feet equal on both sides. The muscular strength in flexion of the legs was fair. Both extension and flexion of the thighs were weak, although the patient could flex and extend the thighs if no resistance was offered. On standing erect there was a forward curvature of the lumbar spine and bulging of the abdomen. He appeared to elevate the hips in walking. The musculature of the calves of the legs appeared large and bulging (Fig. 2). No unusual development in the musculature of the thighs was present, and there was apparently no atrophy of the thigh muscles. He felt pinpoint equally well over both sides

[18] Lewandowsky's Handbuch der Neurologie, Berlin, 1911, Band ii, S. 397.

of the face. There was no anesthesia of the conjunctivæ. He felt pinpoint and light touch over both sides of the back, both sides of the abdomen, and both sides of the thorax. Pinpoint was felt equally well over both lower extremities all over. There was no disturbance of sensation of any form over the arms. The elbow-jerks and knee-jerks were not obtained. The Achilles-jerks were equal and about normal. The conjunctival reflex was present. The umbilical reflex and the cremasteric reflexes were present. Plantar irritation caused plantar flexion of the toes on both sides. He was well-nourished, and an examination of the heart, lungs, and abdominal viscera showed nothing abnormal. The examination of the blood and urine was negative. The blood pressure was 115 mm. Hg. A Wassermann reaction on the blood was reported negative.

Fig. 2.—Pseudohypertrophic muscular dystrophy and optic neuritis.

May 31. Patient was examined by Dr. Walter Parker, who found: Tension O. U., normal. Pupillary reflexes active, normal to direct and consensual light and in accommodation.

Ophthalmoscopic examination: O. D., media clear. Disk margins completely blurred, slightly hyperemic, swollen between 1 and 2 diopters. The temporal side of the disk at the area of the muscular bundle apparently was not swollen. There were some irregular grayish-white changes near the nasal border of the disk, with one or two spots of pigment; these changes were like irregular, inconspicuous branched lines. There was a peculiar stippling of the whole fundus quite marked between the macula and the disk. The veins pulsated. O. S., the disk was swollen, particularly on the nasal side, and there was an oblique position of the disk, the obliquity being so great that the disk seemed to face toward the macula, and the temporal side of the disk was nearly obscured. This was undoubtedly due to an oblique position of the scleral foramen, the optic nerve entering obliquely. The apparent amount of swelling was 3 diopters.

Choroid: There was an area of choroidal change near the nasal border of the disk nearly a disk diameter in size. In this area there was some pigment displacement and a short, crescent-shaped

streak, lighter in color at the outer border of the pigmented area, nearly parallel to the disk border. At the nasal border of the disk there was a small, grayish, rounded area about one-half disk diameter in width, over which the retinal vessels could be distinctly seen. The whole choroid was stippled with grayish pigmentation. There were no pigmentary changes in the periphery of the fundus.

Diagnosis: O. D., optic neuritis. O. S., same as O. D., with localized choroiditis. Two months later the condition was unchanged.

The diagnosis of pseudohypertrophic muscular dystrophy can be made in this case with certainty, but most interesting is the presence, in association with this condition, of a bilateral optic neuritis of a peculiar type. That this is an example of hereditary optic neuritis seems most likely, for the reason that all the details of the ophthalmoscopic findings correspond closely to those described by Hormuth[19] as present in such cases. Furthermore, there was a family history of some similar affection and an absence of any symptoms or signs of intracranial disease to cause optic neuritis and no history or sign of any poisoning.

While the most obvious interest in the cases above recorded lies in questions of diagnosis, they are perhaps more valuable for the evidence they furnish as to the etiology of such conditions. In the cases of dystrophy ordinarily seen there is a tendency to the transmission of the same type of defect from parent to offspring usually a fairly definite type, and the defect apparently is transmitted as are other family traits. If all cases were of that kind there would be little objection to the view that "heredity" was a sufficient etiology, even though we would still be in the dark as to the primary causal factor. When we find a case in which one type in a parent is followed by another type of degeneration in the offspring, or when, as in the last two cases, we find degenerative changes variously localized, it seems more probable that something truly external is acting on the organism, attacking the weaker parts. Generally, true heredity acts in a way which is distinctly opposed to degeneration. According to Lugaro,[20] "Degeneration is a disturbance of physiologic hereditary transmission it is a disease of the hereditary mechanism." The cause of degeneration is something external acting on the organism, and this factor may vary in successive generations. Degeneration therefore is a result of disease of the stock, but a disease that may be curable. If that is true, and the evidence furnished by the above cases seems to confirm such a view, it is of great importance that it be generally recognized.

[19] Beiträg zur Lehre von den Hereditären Schnervenleiden, Hamburg, 1900.
[20] Trans. by Orr and Rows, Modern Problems in Psychiatry, Manchester, 1909.

TWO INSTANCES OF CHRONIC FAMILY JAUNDICE.[1]

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(From the William Pepper Laboratory of Clinical Medicine, University of Pennsylvania, Under the J. Alison Scott Research Fund.)

In June, 1910, Tileston and Griffin,[1] of New Haven, published a report of four families in which this disease appeared in several members of each family. They presented a thorough review of the bibliography of the subject, the major part of which came from the French, though in both the German and English medical literature the condition was by no means ignored. I will take the liberty of giving a short *resume* of their work before presenting my own cases:

Basing their opinions upon their own cases as well as upon those of foreign authors, they conclude that the following points are characteristic of the disease: That it is a chronic, non-obstructive jaundice, with enlargement of the spleen, occurring usually in hereditary form, or in several members of one family, and dating from birth, or first being noticed during adolescence. The icterus is not intense, there are no signs of obstruction of the bile ducts, and symptoms of cholemia, such as itching, xanthemas, and multiple hemorrhages, are lacking. Enlargement of the spleen is almost a constant feature, while enlargement of the liver is unusual.

"Bilious attacks" are extremely common, especially in youth. Headache, diarrhea, and slight fever are occasionally noted. After a day or two the attack passes off, to recur several times in a year. Gall-stone colic is frequently associated, as is, less often, perisplenitis. No hemorrhages are encountered other than epistaxis, which is not uncommon. The jaundice is pronounced in the conjunctiva and the skin of the body is yellow, while the face is of a peculiar characteristic buff color, varying in intensity from time to time, fatigue and worry tending to increase it.

The urine is highly colored, urobilin is present in the majority of cases, as is also urobilinogen, while bile is almost always absent. Urochrome is constantly increased, which accounts for high coloring.

The stools are well-colored, and urobilin and bile are always present, giving marked reactions to corrosive sublimate and Schlesinger's test. Moller has shown the total urobilin excretion in urine and feces to be considerably increased. Constipation is often present.

[1] Read before the Pathological Society of Philadelphia, January 23, 1913.

[2] Amer. Jour. Med. Sci., June, 1910.

The blood-serum always shows the presence of bile-pigment, but not of urobilin. The important feature which gives a clue to the nature of the disease is the decreased resistance of the red blood cells to hemolyzing agents, that is, the increased fragility, which was first discovered by Chauffard. The method for testing for it is as follows: The red blood cells are separated from the plasma, washed, and then placed in a series of test-tubes in which are varying strengths of hypotonic salt solutions, varying from 0.7 per cent. down to 0.36 per cent. NaCl. In normal blood, hemolysis starts at 0.44 per cent., while in this disease it starts almost always at some point higher and not infrequently at 0.6 per cent. or even 0.7 per cent. This marked decrease in resistance is all the more important, because in chronic obstructive jaundice the resistance is normal or increased. Hemolysins have never been found in the blood-serum. A moderate anemia, with red counts between 3,000,000 and 4,000,000, is common. Abnormally high counts have been found. Color-index is usually normal. Average size of red cells is reduced. Reticulation of red cells as shown by the "vital" method of staining is apparently a constant feature. Nucleated red cells and anisocytosis are not rare. Leukocytes are normal.

Pathology. At autopsy liver appears normal, no obstruction of bile ducts, and no cirrhotic changes. Gallstones have been found several times. Spleen enlarged and shows evidences of old perisplenitis. Increase is in pulp, the trabeculæ being, as a rule, not much enlarged. Microscopically there is a marked engorgement, with blood, this being most evident in the pulp. The bone-marrow is found to be in a state of intense reaction.

Etiology. The red cells being more fragile, are readily destroyed, which leads to the anemia and in turn to an increase in free hemoglobin, out of which bile-pigment is made, and hence pleiochromia and icterus. Such a hemolytic icterus has been produced experimentally by Lesné and Ravaut by the injection of hemolytic agents, which is followed by jaundice, increase in size of spleen, and appearance of urobilin, bile, or hemoglobin in urine. Increased destruction of red cells probably takes place in the spleen, and hence its increase in size.

In conclusion, the following cases are presented:

Family No. I.

Case I.—B. A. R., male, aged nineteen years; student. Came to the hospital complaining of yellow discoloration of skin. For three days the patient had noticed a gradually increasing jaundice; there had been no disturbance of digestion nor indiscretion of diet. Bowels were moderately constipated. There was no itching of the skin nor disturbance of vision or other symptoms due to jaundice, except a slow pulse, 58, which was soft and regular; appetite was fair; no fever.

Previous Medical History. Health was always good. Had had three or four attacks of jaundice a year as long as he could remember, but none so marked as this one. Had rheumatism three years before, otherwise negative.

Family History. Grandfather and father had had frequent attacks of jaundice and pain in the upper right abdomen. Sister had somewhat similar attacks, though milder.

Physical Examination. Slender young man of moderate nutrition. Oral mucous membrane pale; tonsils normal. The skin was of a deep yellow tinge; pigment was uniformly distributed over the body; sclera were deeply stained. Lungs and heart were normal. Liver was not palpable; flatness extended from the fifth interspace to the costal margin. The spleen, though not palpable, was considerably enlarged to percussion.

Blood-pressure: Systolic, 110; diastolic, 60. Urine was negative.

Blood Examinations: Hemoglobin, 65 per cent.; red cells, 300,000,000; leukocytes, 7600.

Feces: Clay-colored at beginning of attack for one day, at other times were brown. Occult blood was negative.

Fragility Test: Increased from 0.44 per cent. normal to 0.6 per cent. saline.

Patient's condition remained stationary for five days, after which the jaundice began to clear up. Temperature reached 100° for one day, and then remained normal to subnormal. Pulse rate, 50 to 60. Ten days later he returned for a blood analysis. There was no increase in fragility of erythrocytes at that time. Blood-serum was still greenish yellow, and showed strong bile bands in the spectrum. General condition was much improved, but still showed some jaundice. Seven months later the blood-count was normal. Coagulation time was eight minutes. Fragility increased to 0.48 per cent. NaCl. Bile in the serum. Three months later he was readmitted to the hospital. A tinge of jaundice had remained over the whole of the body. Just previous to admission he was suddenly seized with cramp-like pain in the pit of the stomach, which doubled him up, but it passed away in five minutes. Examination at that time revealed an enlarged and readily palpable spleen and hepatic dulness extending 4 cm. below the ribs in the parasternal line. Stools were dark in color.

Blood Examination: Hemoglobin, 79 per cent; red cells, 3,820,000; leukocytes, 6900. There was some polychromatophilia, also slight anisocytosis and poikilocytosis; red cells were fragile and many were crenated.

Fragility: Hemolysis started at 0.48 per cent. NaCl and was complete at 0.42 per cent.

Serum: Spectroscope showed bile bands. Hemolytic to blood cells of six cases showing normal resistance, but did not affect cells from seven other cases.

CASE II.—N. J. R., father of Case I. Health when presented was good. Had always had a tendency to bilious attacks and headaches. As a boy these would come on after the slighest change in his daily routine, diet, or after any excitement. Attacks began with headache, followed by nausea and vomiting, constipation, and drowsiness for several days. Bowels were constipated, requiring cathartics each day. If they missed a day an attack of headache, etc., would result. After onset of attack, thorough evacuation or vomiting would often bring it to an end. For some years these attacks were followed by mild jaundice. Occasionally, and especially seven or eight years before, he had distinct jaundice. General health not especially affected. Had gained weight in last few years.

Past Medical History. Otherwise negative.

Family History: Father had a tendency to sallowness. Brothers and sisters had no similar trouble. Son had a distinct type of familial trouble. Daughter had slight signs of similar trouble.

Physical Examination. Had an anemic appearance. Eyes were a bit puffy. Slightly sallow complexion. There was no definite jaundice. Liver and spleen were not palpable. Urine and stools were normal. Blood examined for fragility showed normal resistance. Serum was hemolytic to two cases and negative to one.

I did not have an opportunity to examine personally the next two cases:

CASE III.—Grandfather of Case I.

Blood Examination: Red blood cells were fragile to 0.54 per cent. Serum was negative.

CASE IV.—Sister of Case I.

Blood Examination: Erythrocytes showed normal resistance. Serum showed no bile bands. Hemolytic to two cases.

Family No. II.

CASE V.—A. L., male, aged twenty-five years; single. No recent illness. Had diphtheria and measles in childhood. For years had been subject to "bilious attacks," three or four times a year. Was almost always slightly jaundiced, the sclera especially being jaundiced during the "bilious attacks." Had had several attacks of severe pain in gall-bladder region, which he believed to be due to gall-stones. Attacks were always worse in summer or when he was tired out or worried. Pulse was infrequent, often reaching a rate of 54.

Family History. Grandmother was always jaundiced. Father was jaundiced and had "bilious attacks" of the same type as the patient, which were much more frequent in his earlier years. Next to his oldest sister had attacks each month, unassociated with her menses; she was always moderately jaundiced. Stools were frequently clay-colored; urine was dark. General health was

never very good. The next two children were free from jaundice or "bilious attacks." The next three were always slightly jaundiced, and were subject to attacks similar to those of the patient. One had had two severe attacks of gall-stone colic.

Physical Examination. Examination of the patient showed that he had not had an attack for several months except from a slight icteroid hue of skin.

Blood: Hemoglobin, 100 per cent.; red cells, 5,200,000; leukocytes, 4700.

Serum was greenish yellow, and presented strong bile bands in spectroscope. Fragility of erythrocytes started at 0.48 per cent. NaCl. Urine was negative. Stools were dark brown.

A summary of the cases in these families was as follows: The jaundice was in every instance chronic, non-obstructive, and familial in type. In the first family, four members of which had had attacks of varying severity, it may be noted that it extended over three generations, and that the attacks were more frequent and more severe in youth. The spleen was enlarged in each attack, at which times there was a moderate degree of anemia.

Throughout the course of Case I, which we have been able to follow more closely than any of the others, it will be observed that the fragility of the red blood cells ran *pari passu* with the "bilious attacks" and the increase in intensity of jaundice.

Case II did not show any increase in fragility, nor did Case IV, both of which had been free of attacks for some time. Case III showed a lessened resistance of red cells up to 0.54 per cent. NaCl.

The second family presented interesting features, in that three generations were involved and no less than five children in one immediate family were subject to the condition at that time. Owing to the fact that most of the family were living in Canada and New England, I have been unable so far to carry out further studies on the individual cases.

In one point my findings do not confirm those of Tileston and Griffin, as I have found in the serum of three members of this group isohemolysins to be present in ten out of a series of nineteen experiments.

In conclusion, I wish to extend my thanks to Drs. Stengel and Arthur Landry for the opportunity of studying these cases.

CLINICAL AND METABOLIC STUDIES OF A CASE OF HYPOPITUITARISM DUE TO CYST OF THE HYPOPHYSIS WITH INFANTILISM OF THE LORAIN TYPE (SO-CALLED TYPUS FROEHLICH OR ADIPOSO-GENITAL DYSTROPHY OF BARTELS).

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Introduction. Through the efforts of Cushing, Goetsch, and Jacobson considerable light has been thrown on our knowledge of the function of the pituitary gland, especially in its diseased states. Our biochemical knowledge of this gland is scanty, and most of the work conducted has been in relation to the study of the metabolism in animals after extirpation and in acromegaly.

Schiff[1] found no increase in the nitrogen of the urine in acromegaly, but did find an increase in the phosphorus of the feces. Moraczewski[2] found a retention of nitrogen, phosphorus, calcium, magnesium, and chlorine in acromegaly. Oswald[3] found that feeding pituitary extract to a dog had no effect on the nitrogen or phosphorus. Thompson and Johnson[4] found that pituitary substance stimulates metabolism in the dog to an increased degree, as shown by the output of nitrogen, urea, and phosphorus in the urine and also in the decline of the body weight.

Malcolm[5] found that the fresh whole gland increased the output of nitrogen. Benedict and Homans[6] found that the removal of the pituitary gland of dogs produced a tendency to retard the normal growth of the animal and a marked fall of the total metabolism as measured by the carbon-dioxide production. Aschner[7] found that total hypophysectomy in dogs caused a falling off in the nitrogen metabolism and the total metabolism of the fasting animal. The relation of the pituitary body to carbohydrate tolerance has been carefully studied by Goetsch, Cushing, and Jacobson.[8] Von Narbut and others in v. Bechterew's laboratory observed after hypophysectomy a diminution in the carbon-dioxide output, slight diminution in the oxygen intake, an enormous loss of water,

[1] Wien. klin. Woch., 1897, x, 277; Zeitsch. f. klin. Med., 1897, xxxii, Suppl., p. 289.
[2] Zeitsch. klin. Med., 1901, xliii, 336.
[3] Virchow's Archiv, 1902, clxix, 44.
[4] Jour. Phys., 1905, xxxiii, 189.
[5] Ibid., 1904, xxx, 270.
[6] Jour. Med. Research, 1912, xxv, 409.
[7] Wien. klin. Woch., 1909, xxii, 1730, Verhand. d. Deutsch. Gesell. f. Chir., 1910, xxxix, 46.
[8] Johns Hopkins Hosp. Bull., 1911, xxii, 165.

and marked increase in the excretion of nitrogen and phosphorus. Wolf and Sachs[9] found after extirpation of part of the anterior lobe and all of the posterior lobe a distinct lowering of the carbon-dioxide output, and after removal of the anterior lobe only a lowered carbon-dioxide output, while after complete hypophysectomy they found a marked decrease in the carbon-dioxide output and an unusually low nitrogen output.

Edsall and Miller[10] noted a retention of nitrogen and phosphorus in two patients with acromegaly. Franchini[11] found a retention of nitrogen, calcium, and magnesium in a patient with acromegaly; while the sulphur, chlorine, and phosphorus metabolism was normal. Mendel[12] also found a retention of nitrogen and a change in chlorine and phosphorus metabolism. Tauszk and Vas[13] found a slight retention of nitrogen and phosphorus and an increased calcium output. On giving pituitary tablets, no influence was exerted on the general metabolism.

Oberndorfer[14] after careful observations on a patient with acromegaly formed no definite conclusion regarding the character of the metabolism, and was inclined to doubt the finding of definite abnormalities of metabolism in acromegaly. Franchini[15] found extracts of pituitary body of cattle and horse caused a marked loss of calcium, magnesium and phosphorus excretion when injected intravenously into rabbits and guinea-pigs. Mochi[16] found that the subcutaneous injection of pituitary gland caused in rabbits a slight loss of nitrogen and a marked loss of calcium and phosphorus. Medigreceanu and Kristeller[17] studied the general metabolism, with special reference to the mineral metabolism in a patient suffering from acromegaly complicated with glycosuria, and found that the glycosuria followed the usual course of this symptom, while the carbohydrate tolerance was in no way affected by injections of the extract of the anterior lobe of the hypophysis, there was noted a general rise of metabolism after the injection. There also resulted from the injection peculiarities in salt metabolism which could not be interpreted on the basis of the rise of the general metabolism.

None of the experimental work that has been conducted on the question of metabolism in perversions of the pituitary gland can be compared with the study we describe in this paper. As may be noted in the case report, the patient is a classical type of hypopituitarism the opposite of acromegaly (hyperpituitarism), the condition which has been the subject of the several metabolic studies mentioned before.

[9] Proc. Soc. Expt. Biol. and Med., 1910, viii, 36.
[10] Univ. of Penna. Med. Bull., 1903, xvi, 143.
[11] Bioch. Zentral., 1905, p. 522.
[12] Deutsch. med. Woch., 1906, p. 1975.
[13] Jahr. f. Neurol., 1899.
[14] Zeitsch. f. klin. Med., 1908, lxv, 6.
[15] Berl. klin. Woch., 1910, pp. 613, 670, 719.
[16] Riv. di patol. nerv. e ment., 1910, xv, 457.
[17] Jour. Biol. Chem., 1911, ix, 109.

CLINICAL DATA. Hypopituitarism due to cyst of the hypophysis, with progressive bitemporal hemianopsia leading to optic atrophy and infantilism of the Lorain type (so-called typus Froehlich or adiposo-genital dystrophy of Bartels). Kanavel operation.

B. S., male, aged twenty-two years, native of Hungary, unmarried, was admitted to the surgical service of the German Hospital, New York, February 3, 1912.

Family History. The patient has three brothers and three sisters. They are all alive and well, and the men are above the average height. No other member of the family is afflicted in the same manner as the patient. There is no history of consanguinity, alcoholism, lues, tuberculosis, or cancer.

Previous History. The patient had measles and chicken-pox when a child.

Present Illness. When the patient was about ten years old it was noticed that he was not growing normally. Up to this time he had suffered from enuresis, which ceased at his eleventh year. He also began to complain of headaches, which were so severe that they prevented him from playing with other children, and even kept him awake at nights. His eyes watered considerably, and when he was thirteen years old it was discovered that his sight was so poor that he could no read the blackboard at school. Since then his eyesight has been gradually getting worse, so that now he is practically blind. His headaches have continued, and are dull and frontal in character. His physical development has been greatly retarded. He is very irritable. There has never been any indication of sexual power, neither libido, erection, nor ejaculation. There has never been nausea nor vomiting, dizziness, vertigo, loss of consciousness, nor convulsions. He has never shaved. Appetite is poor. Bowels are constipated. Micturition: diurnal 3, nocturnal 1. No polyuria. Some polydipsia. Chief complaints, blindness, headache, arrested development.

Status Praesens. General (Figs. 1 and 2): The patient is a much underdeveloped, but not poorly nourished male. He is 137 cm. (4½ feet) tall and weighs sixty-six pounds. His size is about that of a child of nine or ten years of age. He is somewhat pale and sallow, and his skin is dry. There are no eruptions nor adenopathies. There is a moderate adiposity. The mentality is sluggish, but the patient is not unintelligent nor illogical. There is no trace of imbecility. He talks little, but answers intelligently. The hair on his head is normal, but the patient has not the trace of a beard nor moustache, and no pubic nor axillary hair.

Head: The nose, mouth and pharynx are normal. The ears are rather large, but the hearing is normal. The head measures 55 cm. in circumference. The olfactory nerves are normal, as are all the other cranial nerves, with the exception of the optic. The teeth are in fair condition, and with the exception of the third molars have all erupted. The thyroid is small.

Eyes: The right eye is totally blind. With the left eye the patient can count fingers at one foot. The visual field, however, is much contracted, the temporal half being entirely absent. The pupils are of equal size and are large. There is no consensual nor direct reaction to light from the right eye. In the left eye both reactions are normal. The reaction is much more prompt and

FIG. 1.—Note infantile genitals and absence of facial and pubic hair. Taken before operation.

FIG. 2.—Taken nine months after operation. Orderly is of average height, five feet eleven inches. Note absence of facial deformity from operation.

effectual from the nasal side. The refractive media of both eyes are clear. The disk of the right eye is white and the retinal vessels are well defined. The opthalmoscopic examination of the left eye gives much the same picture. Diagnosis by Dr. Schirmer: primary optic atrophy.

Chest: Small, round, symmetrical. No deformities. No enlargement of thymus.

Lungs: Breathing over left lung normal. Rather harsh breathing, with slightly increased vocal fremitus and slight dulness over the middle lobe of the right lung. Over the upper lobe, posteriorly, on the right side a few crepitant rales may be heard.

Heart: Apex sounds normal. Aortic second somewhat accentuated. Heart action regular, percussion normal.

Abdomen: Soft, symmetrical. No abnormal masses, no areas of tenderness nor rigidity.

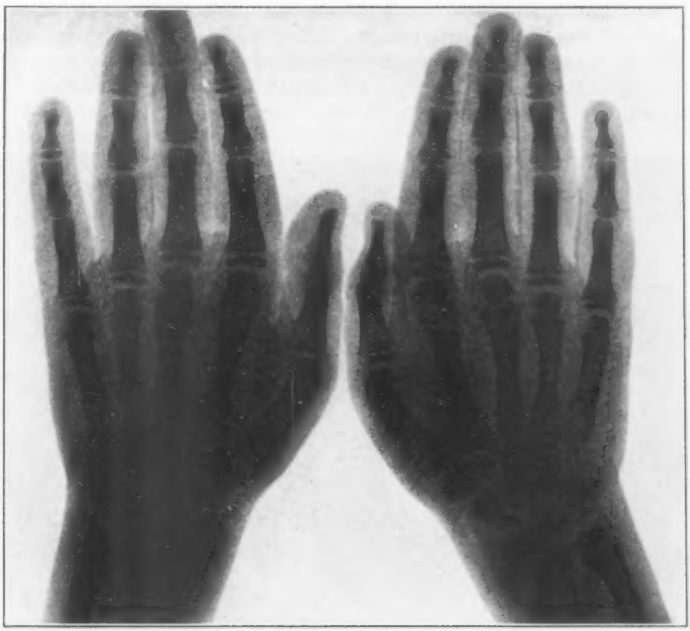

FIG. 3.—*X*-rays of hands and wrists, showing marked arrest of ossification.

Extremities: Hands and feet are small and delicately formed. The fingers are tapering; the nails are well formed, but there are no crescents. The knee-jerks are sluggish. *X*-rays of hand (Fig. 3): The pisiform bones are missing and there are no sesamoid bones. The epiphyses of the phalanges, metacarpals, radius, and ulna are just beginning to unite. The ossification of the bones of the hand corresponds about to that of a boy eleven or twelve years old.

Genital Organs: The penis is small, and the testicles, though present in the scrotum, are exceedingly undeveloped. They measure about 1 cm. in their long diameter. There are no hernias.

Nervous System: Aside from the above-described condition of the eyes there are no abnormalities of the nervous system.

Measurements: From umbilicus to crown, 51 cm.; From umbilicus to soles, 86 cm.; from umbilcus to external malleolus, 77.5 cm., both equal; arms, 22.5 cm., both equal; forearms, 18.5 cm., both equal; from anterior superior spine to internal malleolus, 73.5 cm., both equal; from ulnar styloid to tip of little finger, 14.5 cm., both equal.

Temperature, 99°; pulse, 112, soft and regular; respiration, 24. Blood pressure, 70 mm. of mercury.

Urine: 1260 c.c., acid; amber; clear; specific gravity, 1022; no protein; no sugar. The carbohydrate tolerance is greatly increased, the patient taking as much as 400 grams of glucose without sugar appearing in the urine.

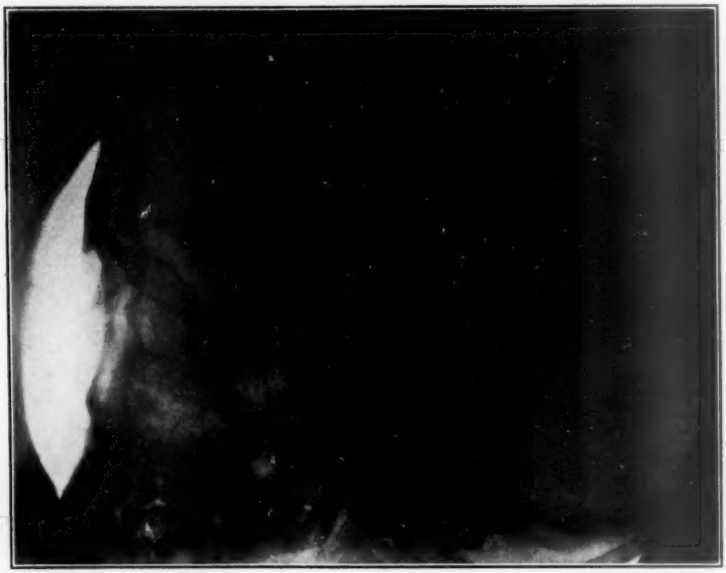

FIG. 4.—*X*-ray of skull, showing erosion of dorsum of sella turcica and posterior clinoid processes.

Blood count: Red corpuscles, 3,900,000; hemoglobin, 55 per cent.; white corpuscles, 10,000; polynuclears, 65 per cent.; large lymphocytes, 1 per cent.; small lymphocytes, 28 per cent.; mononuclears, 5 per cent.; eosinophiles 1 per cent.

The Wassermann reaction is negative.

X-ray examination of the skull (Fig. 4) shows an erosion of the dorsum of the sella turica and of the posterior clinoid processes.

There also seems to be an erosion of the posterior wall of the sphenoidal sinus.

We have here a classic case of infantilism of the Lorain type, with symptoms definitely pointing to a benign tumor, probably a cyst of the hypophysis. The general pressure symptom of headache and the distinct neighborhood signs—namely, the primary optic atrophy, apparently beginning as a bitemporal hemianopsia, and the *x*-ray picture of the skull—made this rather clear. We were obviously dealing with an exquisite case of hypopituitarism beginning in early life. The arrest of body growth and of sexual development, with the moderate adiposity, stamped this case as a typical example of the Froehlich typus or the so-called dystrophia adiposo-genitalis of Bartels. The glandular symptoms are, in the main, due to a deficiency of the anterior lobe of the pituitary gland, although it is evident that the posterior lobe function is also diminished, as indicated, by the high carbohydrate tolerance and the unusually low blood pressure.

In the hope of improving the eyesight and avoiding the threatened total blindness, and incidentally relieving the headaches, operation was decided upon.

Urotropin given and nasal cavity irrigated as a preliminary measure. February 21, 1912, operation by Dr. F. Kammerer. Preliminary inferior tracheotomy. Thyroid gland apparently normal. Ether anesthesia through tracheotomy opening. Pharynx packed with gauze through mouth.

Kanavel's infranasal sublabial trans-sphenoidal approach. A transverse incision was made at the reflexion of the mucous membrane of the upper lip on the alveolar process. The tissues were then elevated and the nasal cavity entered. The cartilage of the septum was incised anteroposteriorly at its junction with the palatal process of the superior maxilla. The cartilage was not removed. The nose was retracted upward. Both inferior and middle turbinates, vomer, and vertical plate of the ethmoid were removed with a rongeur. The bleeding, which was remarkably insignificant, was easily controlled by adrenalin tampons. The anterior wall of the sphenoidal sinus was now clearly seen and removed. The exposure was excellent and there was ample room. As soon as the sinus was opened there was a gush of about an ounce of turbid serous fluid. This was obviously the contents of a cyst, which had eroded the posterior wall of the cell. The fluid was clearly not from the cerebrospinal cavity, as the discharge ceased promptly after it was mopped up and the pulsating dura was seen intact in the depths of the wound.

It was now decided that it would be inadvisable to do anything further as the chief object of the operation had been accomplished namely, the relief of pressure on the chiasm. The cavity was packed with two small iodoform tampons, one of which was led

out through each nostril. The sublabial incision was carefully sutured with silk.

The fluid from the cyst was sterile. It was not possible to obtain sufficient material for proper cytological or chemical examination.

February 23. Tampons removed from nose.

February 24. Tracheotomy tube removed.

February 25. Irrigation of nasal cavity with saline started.

The patient stood the operation well and reacted promptly. Twenty-four hours after operation the temperature rose to 103°; with pulse of 110, and remained so for five days. Then the temperature and pulse gradually came down, but again rose on the ninth day. From this time there were irregular rises and falls of temperature from 103.5° to 100° for nine weeks following the operation. The patient was drowsy, slept most of the time, ate very little, vomited frequently, complained of headache, looked pale, and began to get edema of the face, hands, and feet. He was put on large doses of urotropin.

In spite of constant irrigation of the nasal cavities there was a profuse purulent discharge, especially from the right side. There was no rigidity of the neck, no increased reflexes, and no Kernig symptom.

March 3. Anterior lobe, desiccated pituitary substance, grain j, given three times daily. Discontinued March 8.

April 4. Spinal puncture. 5 c.c. of clear fluid withdrawn. No pressure. Report of Dr. Garbat: No fibrin filament on standing. Very scant sediment after centrifuging. Few cells, but insufficient in number for differential count. Few Gram positive cocci. Globulin reaction negative. Acetic acid test plus. Reduction of Fehling's faint. Cultures: Plate directly from fluid, sterile. Broth tubes from fluid show Staphylococcus albus, evidently a contamination.

The temperature remained high and the symptoms about the same for a week following the spinal puncture. The case made an unfavorable impression, and there seemed little chance of a recovery. Then the purulent discharge from the nose stopped; the temperature dropped to normal and remained so; the headache disappeared; the drowsiness cleared up; the vomiting ceased, and the appetite improved. From this point the patient made a rapid recovery. There had evidently been an extradural suppuration at the site of the old sphenoidal sinus, and this chronic suppurative process, which had been responsible for the septic and pseudo-meningitic symptoms, had now healed.

The eyesight, however, had not improved. If anything it was worse than before the operation. There was practically total blindness. There was perhaps a perception of light in the left eye. No pupillary reaction to light.

June 5. Ophthalmoscopic examination by Dr. Denig showed

optic atrophy of both eyes. The outlines of the disks were sharp, the veins normal, and the arteries a trifle narrow.

The wound in the mouth healed so well that the scar can scarcely be found. There is the slightest trace of a saddle nose as the only external evidence that an operation has been performed. Nasal examination shows a large perforation due to the absence of the bony septum. The turbinates are missing and the cartilaginous septum is deviated to the left. There is a slight serous discharge from the right side.

X-ray examination of the skull reveals no marked changes in the base of the skull.

July 2. The patient was discharged from the hospital, with headaches cured.

He has improved greatly since he left the hospital. He has been examined several times since, the last time on November 20. On November 16, he was presented at the demonstration in the German Hospital to members of the Third Clinical Congress of Surgeons of North America. He looks well, has a good color, and has gained ten pounds in weight since the operation. His headaches are entirely gone and he sleeps through the night, something that he has not done in many years. His appetite is excellent. His bowels are also more regular. His mentality is more active and he is much more talkative. His disposition has changed for the better. He has entirely lost his irritability. As to the sight, there does not seem to be much objective change, though the patient and his mother think there has been some improvement. He claims to be able to see quite well at times. He is able to walk alone on the street, and insists that he sees his way and does not feel it. He claims to see better at dusk. An examination of the eyes by Dr. Schirmer shows that the ophthalmoscopic picture has not changed. The right eye is blind and there is no pupillary reaction. With the left eye the patient can see movements of the hand and the pupil reacts normally. The nose is entirely healed and there is no more discharge. There has been no evidence of growth since the operation. The *x*-ray of the hand shows exactly the same condition as before.

The patient has been put on desiccated pituitary substance (anterior lobe), grains ij, three times a day, after meals.

METABOLIC DATA. *Methods.* Nitrogen determinations were made by the Kjeldahl method, the ammonia by the Folin method, urea by Benedict's new method,[18] uric acid by the Folin-Shaffer method, total sulphur by Benedict's method;[19] creatinin by Folin's method, total sulphates by Folin's method, inorganic sulphates by Folin's method. The ethereal sulphates were estimated by subtracting the inorganic sulphates from the total sulphates and neutral sulphur by subtracting the total sulphate-sulphur from the total sulphur.

[18] Jour. Biol. Chem., 1910, viii, 405.

[19] Ibid., 1909, vi, 363.

Samples of milk used in the diet were analyzed for nitrogen and fat. The nitrogen of the weighed eggs (minus shell) was computed with the aid of the figure given by Koenig (2.008 per cent. nitrogen). The feces were marked off by means of carmine into periods of three days. The fat content of the feces was determined by the method of Kumagawa and Suto.[20]

The patient was placed on Folin's diet,[21] consisting of:

Whole milk	500 c.c.
Cream (18 to 22 per cent. fat)	300 c.c.
Eggs (whole)	450 gm.
Horlick's malted milk	200 gm.
Sugar	20 gm.
Sodium chloride	6 gm.
Water	2100 c.c.

This diet contains approximately 119 gm. protein, 148 gm. fat, 225 gm. carbohydrate, yielding 2787 calories.

The following tables contain the results obtained in this study, and it may readily be noted that the absorption of protein and fat was normal in this individual, while the proportion of nitrogen of the urine as undetermined nitrogen and the proportion of sulphur of the urine as neutral sulphur are regularly much higher than the normal.

TABLE I.—(Nitrogen Partition) Urine.

Date.	Total nitrogen grams.	Urea nitrogen.		Ammonia nitrogen.		Creatinin nitrogen.			Uric acid nitrogen.		Undetermined nitrogen.	
		Grams.	Per cent. of total nitrogen.	Grams.	Per cent. of total nitrogen.	Grams.	Per cent. of total nitrogen.	Co-efficient. Milligrams.	Grams.	Per cent. of total nitrogen.	Grams.	Per cent. of total nitrogen.
June 23	13.0											
June 26	16.1	13.5	83.8	0.36	2.3	0.60	3.8	20	0.20	1.4	1.4	8.7
June 27	16.3	13.3	81.6	0.41	2.5	0.58	3.5	19+	0.24	1.5	1.8	11.0
June 28	15.7	12.6	80.3	0.40	2.5	0.56	3.5	18+	0.26	1.7	1.9	12.1
June 29	15.8	12.9	81.7	0.44	2.7	0.54	3.4	18	0.23	1.5	1.7	10.8
June 30	15.3	12.3	80.5	0.40	2.6	0.50	3.3	16+	0.27	1.7	1.8	11.7
July 1	15.7	12.6	80.2	0.48	3.1	0.55	3.5	18+	0.29	1.9	1.8	11.5

TABLE II.—(Sulphur Partition) Urine.

Date.	Total sulphur grams.	Total sulphate sulphur, grams.	Ethereal sulphate sulphur, grams.	Inorganic sulphate sulphur, grams.	Neutral sulphur, grams.	Sulphate sulphur. Total sulphur. Per cent.	Ethereal sulphate sulphur. Total sulphur. Per cent.	Inorganic sulphate sulphur. Total sulphur. Per cent.	Neutral sulphur. Total sulphur. Per cent.
June 23	0.57	0.45	0.04	0.41	0.12	78.6	6.8	71.8	21.3
June 26	0.41	0.30	0.03	0.27	0.11	72.5	7.2	65.3	27.4
June 27	0.80	0.66	0.06	0.60	0.14	82.4	7.1	75.3	17.5
June 28	0.90	0.69	0.04	0.65	0.21	76.7	4.3	72.4	23.3
June 29	0.90	0.69	0.05	0.64	0.21	76.7	5.5	71.1	23.3
June 30	0.87	0.53	0.05	0.48	0.34	61.7	6.4	55.3	38.3
July 1	0.96	0.66	0.04	0.63	0.30	69.2	4.0	65.2	30.8

[20] Biochem. Zeit., 1908, v. 212.

[21] Amer. Jour. Physiol., 1905, xiii, 45.

TABLE III.—Summary of Data Pertaining to Total Nitrogen and Fat Metabolism.

Date.	Total nitrogen.			Feces.			Fat.	
					Total nitrogen.			
	Ingested grams.	Excreted grams.	Balance grams.	Fat grams.	Found grams.	Per cent. of total nitrogen ingested.	Ingested grams.	Absorbed grams.
June 26 . . .	18.2	17.9	+0.3	2.2	1.8	9.9	140.0	137.8
June 27 . . .	18.6	18.1	+0.5	2.2	1.8	9.7	140.0	137.8
June 28 . . .	18.3	17.5	+0.8	2.2	1.8	9.9	140.0	137.8
June 29 . . .	18.1	17.9	+0.2	1.8	2.1	11.6	146.0	144.2
June 30 . . .	17.6	17.4	+0.2	1.8	2.1	11.9	146.0	144.2
July 1 . . .	17.8	17.8	0.0	1.8	2.1	11.9	146.0	144.2
Total	108.6	106.6	+2.0	12.0	11.7	....	858.0	846.0
Average	18.1	17.7+	+0.33	2.0	1.95	10.8	143.0	141.0

DISCUSSION OF METABOLISM RESULTS. During the six days on the standard diet it may be noted that the patient showed a slight retention of nitrogen, while the absorption of fat and protein was normal in degree. The percentage of the various urinary constituents were normal, with the exception of the neutral sulphur and undetermined nitrogen. The undertermined nitrogen of the urine is made up of substances present in variable amount and difficult to estimate. In this fraction are present various monamino and diamino-acids, hippuric acid, oxyproteic and alloxyproteic acids, allantoin and possibly other substances not yet defined. On a diet yielding about 16 grams of total nitrogen in the urine, Folin has shown that the undetermined nitrogen of normal urine is about 4 per cent. of the total nitrogen. The nature of the neutral sulphur of the urine is also uncertain; it may be made up of the sulphocyanates from the saliva, hydrogen sulphide, cystein, an intermediary compound of normal protein metabolism and taurocarbamic acid from bile. Traces of chondroitin-sulphuric acid and, oxyproteic acids also help make up the neutral sulphur content of the urine. Cystin, if present, would also increase the neutral sulphur. Folin has shown that the neutral sulphur of the urine is made up of substances, which in the main are independent of the total amount of sulphur eliminated or of protein catabolized and variations in the neutral sulphur of the urine, must be regarded as showing presence of abnormal metabolic processes, which are not associated with variations in the other types of urinary sulphur. On the diet given to this patient the neutral sulphur should not normally be higher than 10 to 12 per cent. of the total urinary sulphur.

We therefore have in this case a marked perversion of some metabolic process leading to high and abnormal percentages of the neutral sulphur and undertermined nitrogen of the urine. Our knowledge of these two groups of substances is very meager, and it would be unwise at present to attempt any specific explanation of this anomaly.

THE DIAGNOSIS OF GASTRIC ULCER.[1]

By J. Russell Verbrycke, Jr., M.D.,
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Ulcer of the stomach is only diagnosticated about one-third as often as it should be. This has been proved at autopsy time and again, and can be shown clinically when routine employment of the more exact methods for the recognition of ulcer is tried.

In Cabot's report of the analysis of 3000 cases coming to autopsy at the Massachusetts General Hospital, he claims that but 36 per cent. of the ulcers of the stomach were correctly diagnosticated. It should be remembered, too, that this represents work of men who are well up at the head of the internists of the country.

Something is wrong. What is it? Are the means at our command for the diagnosis of ulcer inadequate? The writer thinks not. He believes that at least 90 per cent. of the cases should be recognized with our present diagnostic methods though the remainder will probably continue to baffle us.

There are several reasons for the great number of ulcers escaping detection. The average physician does not suspect the enormous number of dyspeptics the cause of whose trouble lies in ulcer of the stomach or duodenum. He looks for the former text-book symptoms and does not find them. The entire subject should be and will be rewritten.

Germany, feeling the need for more exact knowledge concerning ulcer, has appointed a committee of leading clinicians to investigate principally the etiology, and a subcommittee has been appointed in this country, but as they accept for their records only those cases which have been proved by operation or autopsy, the great mass of cases, the ones in fact that are the most difficult of diagnosis, will not be included, and we will be helped in the problem but little.

The real signs of ulcer are not tested for often enough in patients who have not the unmistakable ear-marks of ulcer. We want early diagnoses before the typical and evident symptoms appear.

It is generally accepted that there is an acute or so-called medical ulcer and the chronic indurated ulcer. There can be little doubt that there is at least a third class, chronic non-indurated ulcer, perhaps an intermediary stage or a forerunner of the indurated ulcer. Such a condition may persist for years and not be recognized. The average duration of the cases operated upon by the Mayos has been twelve and one-half years. Where have these patients been during all this time? Again the writer wishes to

[1] Read at Symposium on Gastric Ulcer, joint meeting of Medical Societies of Georgetown University and George Washington University, January 11, 1913.

emphasize the importance of the early diagnosis at the very beginning of this long stretch.

The writer will not consider differential diagnosis because of lack of space. Indeed, it is not necessary if one bears in mind the diagnostic points of ulcer itself and remembers that another trouble may be present at the same time. For instance, if a patient undoubtedly has gallstones he may also have ulcer, since the two conditions are often concomitant.

The means at our command for the diagnosis of ulcer come under four headings: (1) Consideration of the history and symptomatology; (2) physical examination; (3) special tests and laboratory aids; (4) the therapeutic test.

History and Symptomatology. The history and symptoms complained of by the patient are typical in but few cases, notably, the chronic surgical ulcers and some of the acute ulcers. Most symptoms may be simulated by other conditions, and on the other hand for every ulcer with characteristic symptoms there are probably a couple of others with few if any of the symptoms which might be expected.

Pain may or may not be present. There is no characteristic sort of pain in ulcer. Perhaps the variety of pain which will be less apt to mislead than any other is that running through from front to back, expressed by patients "as if a stick were run through the body and then twisted around." This particular sort of pain is of some diagnostic importance, but in comparison with the whole number of ulcer cases is met with but rarely. It may be said that there are only two characteristic points about the pain in ulcer: its time of occurrence and the method of its relief. The pain appears at a fixed time after meals, different in different individuals, but always the same in the one patient. The pain is relieved by more food, alkalies, or vomiting.

Various acid symptoms of heart burn, pyrosis, regurgitation, etc., are all common in ulcer, and doubtless many of the "sour stomachs" if studied closer would be found to be due to ulcer, but these symptoms are by no means characteristic of ulcer.

Hematemesis, one of the old cardinal symptoms, probably does not occur in 10 per cent. of the patients. As Cabot remarks, it is decidedly more characteristic of cirrhosis of the liver than of ulcer.

Even nausea and vomiting, while undoubtedly present many times, do not occur in one-half of the ulcer patients, and these symptoms even when present have absolutely no value unless it be in the effect of the vomiting in stopping pain.

There are two points, however, in the consideration of the history which are of decided value in the diagnosis of indurated ulcer. There is exhibited a certain periodicity in some of these cases. The patient may have been miserable for a couple of months,

when suddenly with no apparent reason and often in spite of some gross indiscretion he will be completely relieved of all symptoms and enjoy good health for a varying period of days, weeks, or months. These periods of euphoria and misery alternate to the patient's complete mistification, and in stating their history he will frequently comment on this with expressions of surprise.

The other important point is that when pain is at its height all other symptoms from which the patient is suffering are apt to be increased also, and that they tend to be relieved by the same measures which stop the pain.

It is surprising how frequent are the mistakes even in these chronic ulcers, the easiest of any to diagnosticate, simply because the physician still looks for pain, vomiting, and hematemesis, and overlooks the periodicity of symptoms and the manner of their relief. Within the past month the writer saw two chronic ulcers, one of twelve years' duration and the other of seven years. The diagnosis was easy in both cases after talking with the patients for about five minutes, and was corroborated by tests and later by operation, and yet one of these patients had consulted several physicians and had been under observation in the ward of one of the city hospitals for three weeks, while the other had in the course of the twelve years consulted as many physicians and only one of the number had ever suggested ulcer, a surgeon in Denver.

Physical Examination. The results of physical examination are, on the whole, somewhat more reliable than the consideration of the history and symptoms.

There is usually present at some time a tender point at some spot in the epigastrium or at the eighth dorsal vertebra behind, or both. The tenderness is often slight and is at times absent. In order to be of diagnostic value the tenderness should always be in the same place, and there should be but one spot. Points of marked tenderness can often be found in enteroptotic nervous women, but usually further examination will reveal that there are several of these spots.

Muscle spasm and rigidity are, when present, but further evidence of tenderness.

Special Tests and Laboratory Aids. The special tests and laboratory aids afford us the most exact means of diagnosticating ulcer. The writer attaches more importance to the test for occult blood than to any of the others. Occult bleeding occurs in the large majority of all ulcers regardless of the duration or variety. The bleeding is, however, characteristically intermittent, and for that reason several examinations under varying conditions should be made. The benzidine reaction is the best of which the writer has knowledge. Being as delicate as it is, several precautions are necessary. Test-tubes should be absolutely clean. The patient may be on regular diet when the first examination is made,

but if a positive test is secured he should then be put on a meat-free diet for several days, to exclude the blood from the meat and the test repeated. If a positive test is then obtained, all bleeding points, as hemorrhoids, bleeding gums, etc., should be excluded. If negative results are obtained in a case which has a suspicion of ulcer the patient should be placed upon a coarse and irritating cellulose but meat-free diet for a couple of days. The writer never feels certain of a diagnosis of ulcer without the presence of occult bleeding.

Hyperacidity is found in a large proportion of all patients with ulcer, but is not to be compared in value to the presence of hypersecretion, which is a valuable indication, though not by any means pathognomonic of ulceration.

Meunier rinses the stomach out with 1 per cent. acetic acid solution and tests the rinse water for blood. This procedure has been of service to the writer in several cases, but it is an admitted fact that the test for occult blood in the stomach contents has not the same value as for that in the stool. The tube itself is too apt to produce small abrasions of the mucosa.

The *x*-rays are of undoubted value in the diagnosis of ulcer, and may be necessary in some doubtful cases, but has several manifest disadvantages. It is an expensive procedure and the average patient cannot afford it. Not only is it sometimes impossible to get pictures taken, except in the largest cities, but the interpretation of the findings requires the services of an expert of considerable experience in stomach *x*-ray work.

One of the latest and most ingenious methods which has been devised for the diagnosis of ulcer of the stomach and duodenum is the thread-impregnation test of Einhorn. The writer has used this test from the time it was first described, and has had large experience with it, and yet even now holds it more or less *sub judice*. As a test for the localization of ulcer it is well-nigh perfect. As a means of diagnosis it has been the writer's experience that certain positive threads are almost infallible, but he does not believe that a stained thread always denotes ulcer even in the absence of cirrhosis and cancer.

The technique of the test has been already described several times by Einhorn, Morgan, and the writer, so that it will not be again given. It will suffice to say that a silk thread, swallowed at night by the patient and retained all night, rubs to and fro against the ulcer and causes it to ooze blood so that a stain is left on the thread and is plainly visible when the thread is pulled up in the morning.

The writer has found that those threads with a plain mark or two marks denoting the rim of an ulcer, with an unstained portion between, are never misleading. Again, any sort of a stain which is present on two or more threads at exactly the same point is a sure

indication of ulcer. On the other hand, the writer cannot believe that the many instances of diffuse stained thread are all caused by ulceration. A stained thread, however, always does denote a pathologic condition of the mucous membrane, if not ulceration, then a soft, spongy state. It is probably these same cases which often have the wash water from lavage returned red with blood, simply from the irritation of the tube, when we can be almost sure that no ulcer is present.

THERAPEUTIC TEST. Some cases will continue to defy our ability to make a diagnosis, and these will have to be treated as ulcers and the results of treatment noted. The writer has treated some patients for weeks for other conditions, always bearing in mind the possibility of ulcer, while others he has treated as ulcer, on suspicion, never feeling sure as to the diagnosis, and has been rewarded by the therapeutic test confirming his suspicions.

In conclusion, there are several combinations which practically assure a diagnosis:

Tender point with occult blood.
Hypersecretion with tender point.
Hypersecretion with occult blood.
Tender point with repeated positive thread tests.
Tender point with hematemesis.
Hematemesis with hypersecretion.
Hypersecretion with positive thread tests.

REVIEWS

THE MODERN TREATMENT OF NERVOUS AND MENTAL DISEASES BY AMERICAN AND BRITISH AUTHORS. Edited by WILLIAM A. WHITE, M.D., Superintendent of the Government Hospital for the Insane, Washington, D. C., Professor of Nervous and Mental Diseases in the Georgetown University, and SMITH ELY JELLIFFE, A.M., M.D., Ph.D., Adjunct Professor of Diseases of the Mind and Nervous System in the Post-graduate Medical School and Hospital, New York. 2 volumes; pp. 1630; illustrated. Philadelphia and New York: Lea & Febiger, 1913.

THIS is indeed a modern "treatment." The family doctor has for years been asked to buy treatments of nervous and mental diseases, only to be confronted by the same old story of massage, electricity, hydrotherapy, and rest cures until he has associated these methods as the only ones which can possibly be employed for the cure of those who are unfortunate enough to come into the hands of a neurologist. It is therefore high time for this book. Indeed the authors are to be admired for their courage in presenting a work of this sort.

We have in these two volumes monographs by different men in this country and England which apparently have been edited. Rather an unusual feature in volumes by many authors. The subject matter has been well selected. The publishers have done their work well, although the illustrations leave much to be desired, not because those that are present are not good, but because there are not enough of them. To the reviewer, no book is complete without free illustrations, for it is the best way to teach anything.

Such unusual subjects are discussed as eugenics and heredity, educational and sexual problems, the feeble-minded and their treatment, delinquency, immigration, and the mixture of races, and then what is certainly very unusual, because these subjects have always been considered incurable, such diseases as dementia præcox, maniac depressive psychoses, paranoia and paranoid states, presenile conditions, and then nervous disorders occurring in prisons and in military duty. All this in the first volume.

The second volume contains the usual diseases of the nervous system. It is difficult to pick out any one chapter or any one subject for special mention because they are nearly all good.

What should be most highly praised is the selection of the subjects discussed, for, as is well said in the introduction, "this book begins where others leave off."

It is not at all, therefore, surprising in such a book as this that sexual problems are treated as if they really occurred in the human race, instead of apologizing for mentioning them. Not at all surprising is the fact that the neuroses are treated from the Freud standpoint and too much tabooed subject of psychanalysis is adequately discussed. Neither is it surprising that in the discussion of insanity instead of fitting in all symptoms to certain diseases, a psychological standard is adopted. Altogether one finds a great deal of joy and hope in the future of neurology in such a work as this.

T. H. W.

LIFE AND LETTERS OF DR. WILLIAM BEAUMONT. By JESSE S. MYER, M.D., Associate in Medicine, Washington University. Pp. 317; 58 illustrations. St. Louis: C. V. Mosby Co., 1912.

THE story of Alexis St. Martin and Dr. Beaumont has always had a fascination for those who have heard only a fragment, but we are now in possession of a monumental work, which being read, must deepen our admiration for this American pioneer, and his remarkable physiological researches. The zeal with which Beaumont pursued his studies and his recreant and totally worthless subject, are told with a simplicity and directness whose reward is the strong appeal it makes. Dr. Myer deserves the highest commendation for his compilation and the difficulty of his undertaking can be appreciated by any one who will read his preface. The book is replete with suitable illustrations, and letters of Beaumont are preserved in their original form thereby giving an atmosphere to the book which is most entertaining. What a contrast the difficulty and primitiveness of Beaumont's researches and technique bear to the modern facilities for undertaking a physiological problem! We recommend to all this exceptionally good biography.

E. H. G.

A TEXT BOOK OF BIOLOGY. For students in medical, technical, and general courses. By WILLIAM MARTIN SMALLWOOD, Ph. D., (Harvard). Professor of Comparative Anatomy in the Liberal Arts College of Syracuse University. Pp. 285; 243 engravings and 13 plates. Philadelphia and New York: Lea & Febiger, 1913.

THIS book is one of the newer forms of texts in which the attempt is made to give the general principles underlying the structure,

behavior, and relations of organisms rather than a catolog and arrangement of their forms. But two chapters of the eighteen refer to classification at all and in these the principles of taxonomy are dwelt upon more than the results of their application. An earnest attempt is made to cover the biological field, but its great extent and the limits of the book make the treatment of many subjects necessarily brief. In some places there is apparent a lack of careful judgment of values. This shows itself, for example, in the use of some highly specialized illustrations, taken from monographs, and in certain quotations from technical papers the language of which is not entirely suited to an elementary text.

Despite these minor weaknesses, however, the book has much to commend it, especially to those looking toward a medical career. It considers modern biological problems from a real scientific standpoint and presents essential facts in their direct bearing upon everyday life. There are eighteen chapters of which the first thirteen, occupying 163 of the 285 pages, deal with general questions of morphology and physiology and the small amount of taxonomy. The remainder are devoted to more special topics under the titles "Some biological adaptations" (parasitism); "Some biological factors in disease," "Evolution." "Variation-heredity," "Animal behavior and its relation to mind." The longest chapter is the one dealing with the factors of disease and the next in length is the one concerning variation and heredity. Although the subject matter of these two chapters is widely different in some respects, the treatment of each is strictly scientific and will doubtless prove of great interest to medical men. C. A. McC.

THE SURGICAL CLINICS OF JOHN B. MURPHY, M.D., AT MERCY HOSPITAL, CHICAGO. June, 1913. Pp. 185; 62 illustrations and a colored frontispiece. Philadelphia and London: W. B. Saunders Company, 1913.

THIS number of Murphy's *Clinics* contains the usual variety of interesting surgical matter, ranging from such topics as intestinal obstruction from gall-stones and procidentia uteri, to ankylosis of the jaw and fracture of the neck of the femur. An interesting clinical lecture and series of operations by Dr. Albee of New York City is included, dealing chiefly with bone transplantation in cases of Pott's disease; but Dr. Albee does not neglect the wider applications of bone transplantation to ununited fractures and congenital and acquired deformities of the limbs. The two most interesting bone cases reported by Dr. Murphy are one for arthroplasty of the hip for ankylosis the result of tuberculous disease,

and an operation for ununited fracture of the neck of the femur. The former condition, tuberculous ankylosis, is one which most surgeons, including the reviewer, have considered not suitable for arthroplasty, on account of the danger of stirring up the old disease; the motto *μὴ κίνειν ραμιαχίναν* or *quieta non movere* being in no class of cases more important than in these. And it is interesting to see that Dr. Murphy after beginning the operation found an abscess close to the hip-joint, and left his patient, at last reports, with suppurating sinuses. It will be of much importance to learn the final result. A. P. C. A.

DIET AND HYGIENE IN DISEASES OF THE SKIN. By L. DUNCAN BULKLEY, A.M., M.D., Physician to the New York Skin and Cancer Hospital; Consulting Physician to the New York Hospital. Pp. 194. New York: Paul B. Hoeber, 1913.

THERE is much to commend and recommend, also several things to criticize, in the publication of Bulkley's book on the diet and hygiene as they affect the skin. Every one should realize the importance of the generalities, emphasized in the first portion of the volume, as to the quantity, the quality, and the mode of preparation of the food, the time and the method of consumption, the nervous element, fatigue and irregular eating which may give rise to the improper digestion of the same. The value of this portion of the volume cannot be too strongly emphasized. The author relies, however, too much on urinary examinations to prove the metabolism of the individual, without ascertaining sufficiently the amount and the character of the food ingested. He considers that the greatest fault with most individuals with diseases of the skin consists in too great a quantity of nitrogen in the food. A rice diet is strongly advocated in certain cases of acute eczema and other inflammatory conditions of the skin, including erythema multiforme. A "wheat-jelly" is strongly recommended as a diet in infantile eczema. Bulkley makes the statement that a vegetarian diet is both helpful, curative, and preventive in psoriasis. Many, if not most, dermatologists will disagree with him in this statement. Most authorities will hardly agree with his belief in the effectiveness of a vegetarian regimen in mycosis fungoides, epithelioma, or alopecia.

The second portion of the volume is devoted to the hygiene of the individual and to others than the patient. The subjects mentioned are all more or less important, such as regularity of the bowels, sleep, exercise, the irritation of certain occupations, the clothing, bathing including medicated baths, and so on. Two

interesting tables are presented; the first, contains articles of food and their fuel value and the second, edible nutrients and their fuel values. F. C. K.

Diseases of the Ear. By Philip D. Kerrison, M.D., Professor of Otology, New York Polyclinic Medical School and Hospital, Junior Aural Surgeon to the Manhattan Eye, Ear and Throat Hospital; Aural Surgeon to the Willard Parker Hospital, etc. Pp. 588; 333 illustrations. Philadelphia: J. B. Lippincott, 1913.

In presenting this excellent addition to the list of otological text-books the author has taken into full consideration the rapid strides otology has taken in the last few years. Emphasis is laid upon the fact that the otological surgeon has passed far beyond his former rather narrow field and has become a general intracranial surgeon.

Suppurative lesion of the brain and meninges cover nearly two hundred pages, far more space than is usually allotted to these subjects. The intricate surgery and physiology of the labrynth are described in great detail. The chapter on serum therapy in the treatment of aural disease, embracing autogenous vaccines and the His leukocyte extract, is a distinct innovation.

In the arrangement of the subject matter the usual time honored customs have been disregarded, prominence being given to the practical side of otology and not to anatomical sequence. The illustrations are numerous, and most of them are new, being taken from original drawings by the author.

The entire work well represents the most modern otological theories, with the preservation and rearrangement of well established facts. B. D. P.

Nervous and Mental Diseases. For Students and Practitioners. By Charles S. Potts, M.D., Professor of Neurology in the Medico-Chirurgical College of Philadelphia, Neurologist to the Philadelphia Hospital, Formerly Associate in Neurology in the University of Pennsylvania. Third edition, revised and enlarged. Pp. 610; 141 illustrations and 6 plates. Philadelphia and New York: Lea & Febiger, 1913.

The third edition of Dr. Potts' book on Nervous and Mental Diseases follows along the same plane of excellence noted in his former editions. The book is well printed and well illustrated,

and a good example of the bookmaker's craft. Many new features have been added, such as the importance of the Wassermann reaction, the latest view of tic, and short descriptions of some of the newer symptom-complexes, myotonia atrophica, progressive lenticular degeneration of Wilson, etc.

The chapter on symptomatology is one especially to be commended. This contains features well arranged for the student in his first study of this subject. It is unfortunate that in the chapter on hysteria, Freud's ideas are dismissed in a single paragraph.

The book approaches in some ways many of the larger works on Neurology, but misses the philosophic grasp which lends so much to the unity of such a subject. Nevertheless the work should prove valuable to the student and general practioner, both for its conciseness and lucidity. S. L.

SELECTED PAPERS ON HYSTERIA AND OTHER PSYCHONEUROSES. By SIGMUND FREUD, Vienna. Authorized translation by A. A. BRILL, M.D., Ph.B., Chief of Nervous Department, Bronx Hospital and Dispensary. Second edition. Pp. 215. New York: The Journal of Nervous and Mental Disease Publishing Co.

THIS is the second edition, the only change consisting of two chapters, one on wild psycho-analysis and the other on the future chances of psycho-analytic therapy.

The mere fact that a second edition has appeared within a year of the publication of the first is an indication of the need of this work and the growth of Freud's teaching in this country. Since the appearance of the first edition many papers upon this subject have been published, and a National Society for the Study of Psycho-Analytic Method has been formed. While all this indicates that psycho-analysis is better recognized, it has not by any means minimized the spirit of antagonism which it has aroused. The reader is referred to the review of the first edition which appeared in a previous number of this JOURNAL. T. H. W.

FOR AND AGAINST EXPERIMENTS ON ANIMALS: EVIDENCE BEFORE THE ROYAL COMMISSION ON VIVISECTION. By STEPHEN PAGET, F.R.C.S., Hon. Secretary Research Defense Society. New York: Paul B. Hoeber.

THIS book should prove to be of great value to all who are interested in the important question of vivisection, which is being constantly brought before the public.

Paget, from his position as Hon. Secretary Research Defense Society has been able to obtain the evidence of both antivisectionists and various investigators. He carefully shows the remarkable benefits which have been given to mankind during the last twenty or more years, and which were alone obtainable through experiments upon the lower animals. Innumerable instances are quoted, as the discovery by Lister of antisepsis to be followed later by asepsis, the Pasteur treatment of hydrophobia, diphtheria antitoxin, and many other prophylactic and curative methods, all of which were accomplished solely through experiments on animals, thus utterly refuting the statement which is continually being advanced by the antivivisectionists that no benefits to humanity have ever been derived by such means.

Another point advanced by those who would abolish all work upon animals, and refuted by the other side, is the excessive cruelty and suffering to which the animal is subjected. The testimony, however, before the Royal Commission, given by such men as Starling, Cushing, and Sir Victor Horsley showed that from their wide experience in the subject they had found that the greatest care is always exercised to prevent any suffering, the animals always being completely anesthetized before they are operated on, and every known method being employed to prevent postoperative discomfort, and to this evidence the opposing side was unable to prove one authentic case to the contrary.

Taken as a whole, the book gives a clear, concise, and unprejudiced statement of the findings on both sides of this very important subject, and should help once and for all to settle the question in this country, where every so often a movement is brought forward endeavoring to check all scientific reasearch by limiting experiments on animals. F. P., Jr.

A Practical Medical Dictionary. By Thomas Lathrop Stedman, A.M., M.D., Editor of *Twentieth Century Practice of Medicine;* Editor of the *Medical Record.* Second edition. Pp. 1028. Illustrated. New York: William Wood & Company.

The second edition of this standard dictionary from the scholarly pen of Dr. Stedman contains many admirable features. There have been incorporated in the text life insurance, dental, veterinary, botanical, electrical, homeopathic, and eclectic terms; but of particular value has been the inclusion of eponymus terms in their alphabetical order. With such terms there has been appended a short biographical sketch of the persons whose names have been applied to diseases, symptoms, signs, etc. A list of the mineral springs of America and Europe, with information as to their

chemistry and therapeutic value has also been incorporated. The pharmaceutical preparations of the United States, British, and National pharmacopœias have been added.

In the spelling Dr. Stedman has seen fit to countenance the simpler forms with consequent elimination of the diphthong æ and œ, a method of spelling which is being universally employed in this country but to which British physicians object.

The book fulfils all the demands of a medical dictionary for fulness and accuracy and can be unreservedly recommended as a thorough, exact, and careful compilation. J. H. M.

THE OCULAR MUSCLES, A PRACTICAL HANDBOOK ON THE MUSCULAR ANOMALIES OF THE EYE. By HOWARD F. HANSELL, A.M., M.D., Professor of Ophthalmology in the Jefferson Medical College; and WENDELL REBER, M.D., Professor of Ophthalmology in the Medical Department of Temple University. Second edition. Pp. 223; 3 plates and 82 illustrations. Philadelphia: P. Blakiston's Son & Co.

THE intelligent reader after mastering the contents of this book will have little to learn of the practical in the matter of the ocular muscles. There is naturally much of the theoretical which is necessarily omitted; a fuller discussion of the refraction by prisms with an elementary exposition of the mathematical theory would have been in place, but the authors have laid emphasis more especially upon the needs of those for whom the book seems intended. The practitioner who is interested in the anomalies of the ocular muscles will find this handbook a clear and reliable guide to which he can confidently turn.

It is particularly satisfactory to note the sane views the writers take on the subject of heterophoria. A half-dozen purely ocular symptoms are clearly stated. Of the reflex symptoms, headaches —with nausea, vomiting, and vertigo—are very properly connected with heterophoria, but no extravagant claims are made. As regards epilepsy, we quote: "We believe it is the latter class of cases (vertigo with momentary unconsciousness, etc.) that are vaunted by many as instances of essential epilepsy partially or even entirely curable by eye-treatment alone."

Operative treatment is recommended as a last resort in esophoria; in exorphoria, the choice is between tenotomy and advancement when other measures have failed. While in hyperphoria, operation is narrowed down to where the deviation tendency is constant and when all tests agree in showing marked over- or under-action of one set of elevators or depressors, the use of prisms and exercise having been without avail. T. B. S.

DIE CHIURGISCHEN UNTERSUCHUNGS-METHODEN. By PROFESSOR DR. HUBERT GEBBELE. Pp. 184; 154 illustrations. Munich: J. F. Lehmanns.

GEBBELE has condensed the essentials of surgical diagnosis into a small volume. After a page and a half devoted to the importance of the history and the method of taking it, he considers the various physical signs elicited by inspection, palpation, percussion and auscultation. The passage of sounds into the esophagus and stomach, the rectum, and the urethra, and the diagnostic indications for the hollow needle and exploratory incision, are discussed. Other chapters are given to the methods of examining the secretions and excretions, and the blood. Serodiagnosis, endoscopy, and radiography are also dealt with. The author aims at stimulating independent, systematic investigation and does not enumerate in detail the symptoms of the conditions described and illustrated. The book serves well the purpose for which it was written, and will be useful not only to the young but the older physicians as well. T. T. T.

A PRACTICAL TEXT-BOOK OF THE DISEASES OF WOMEN. By ARTHUR H. N. LEWERS, M.D., Senior Obstetric Physician to the London Hospital. Seventh edition; pp. 530. New York: Paul B. Hoeber, 1912.

THIS work doubtless serves as a text-book to the students taught by the author, and as such will fulfill its purpose admirably. It is, however, too markedly an expression of the personal opinions of the author, to the exclusion of other and well tried methods of treatment, ever to be of great value to students other than his own. The first chapter is excellent and contains a detailed description of the methods of taking the history and examination of a patient, which could well be imitated by other text-books on this and similar subjects. It is regrettable that as much cannot be said for the remainder of the book. Here, when we have long ago given up such methods as archaic, it seems strange to find recommendations to dilate the cervix by Higar's bougies and by tents; to recommend the Tait operation as the only method of perineorrhaphy; to find no mention of the Schatz metranoikter in the treatment of dysmenorrhea and sterility, to mention only a few of the more obvious points. The book is based upon a small experience (1083 abdominal sections in eleven years; 2 a week), and will hardly appeal strongly to the profession in this country. J. C. H.

THE TREATMENT OF SHORT SIGHT. AN ELABORATION OF THE LECTURE GIVEN EACH YEAR TO HIS STUDENTS. By PROFESSOR HIRSCHBERG. Translated into English by G. L. JOHNSON. Pp. 123; 10 illustrations. New York: Rebman Co.

ANY discussion upon this subject by one who has had the opportunity to observe this condition in a large number of patients is, of course, worthy of thoughtful consideration. Professor Hirschberg, by reason of his residence in Germany, where myopia is so unusually prevalent, and because of his many years of practice, has thoroughly studied this condition. Being an observer of unusual acuteness, his presentation of this subject has resulted in a real and valuable contribution to ophthalmic literature.

So vivid is his portrayal of myopia as it progresses through the consecutive stages of the pernicious form, that the reader can, in a short space of time, have a grasp of the subject that would perhaps take years of observation of an individual case to duplicate.

The reader will be impressed with the sincerity of the author's convictions, and will find a second reading of this unique book time well expended.

B. F. B., JR.

STUDIES IN CANCER AND ALLIED SUBJECTS. PATHOLOGY. Conducted under the George Crocker Special Research Fund at Columbia University. Volume II; pp. 267; 32 plates and numerous charts. New York: Columbia University Press.

THIS report is made up of a series of twenty-seven articles, all of which have been published independently. The workers who have furnished most of the material are Isaac Levin, and Robert A. Lambert, the former having as his associate in several articles; M. J. Sittenfeld, Lambert being assisted by Frederick M. Hanes. Robert T. Frank has contributed two articles, in one of which he was assisted by A. Unger. The studies deal with a wide variety of the phases of cancer study, including a consideration of ethnological relations, heredity, etiology, immunity, metastasis formation, biological chemistry, and tissue cultivation. Nearly all the studies are experimental in nature, and present a careful analysis and consideration of the new facts learned.

A valuable feature of the work is W. G. MacCallum's introduction, which briefly summarizes, in an admirable fashion, our modern views as to the etiology, biology, and therapy of cancer.

H. T. K.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Research on Pellagra.—G. VOLPINO (*Pathologica*, 1913, v, 174) finds that the intramuscular injection into pellagrins of the aqueous extract of spoiled maize causes fever, nervous and psychic symptoms, vomiting, diarrhea, and tachycardia. The similar injection of extracts of good maize causes none of these symptoms. The active principle of the potent extract is carried down by an alcoholic precipitate, and is active in doses of 1 c.c. of a 0.5 per cent. solution. Such inoculations cause reactions in 90 per cent. of pellagrous subjects, and in about 20 per cent. of the non-pellagrous; the reaction in the latter group, he thinks may be due to eating of maize or other cereals, or it may be an evidence of "latent pellagra." Volpino designates the reagent "pellagrogenina;" it is non-toxic to rabbits fed in the usual manner, but to maize-fed rabbits, 1 c.c. of a 1 per cent. solution is fatal within twenty-four hours. The injections were made intraperitoneally. He also finds that guinea-pigs fed mainly on maize die after being injected with 1 c.c. of the serum of a pellagrin, whereas normally fed pigs are in no way affected. Maize-fed guinea-pigs treated several times with pellagrogenina readily survive the subsequent injection of serum from pellagrous patients. No microörganisms could be demonstrated microscopically or by cultural methods.

Lipoid Chemistry of the Blood—The discovery that cholesterin may occur in the blood in a free form is not unimportant, in view of the known neutralizing action it exerts upon saponin and cobra venom hemolysis. It may well be that it has a similar effect in the body upon the toxins of various acute infections. Rohmann believes that a relative increase of the free over the bound cholesterin is characteristic

of sera giving a positive Wassermann reaction, while Peritz claims to have found a constant increase of lecithin in the sera of tabetics, and ascribes to this the positive reactions. BÜRGER AND BEUMER (*Berl. klin. Woch.*, 1913, l, 112) have investigated the sera of 21 individuals suffering from a variety of conditions. Serum was dried at 40° C. and extracted for two days with alcohol and chloroform; after weighing, the extracts were redissolved in ether and reprecipitated with acetone. The filtrate was divided into two portions; in one the cholesterin was thrown down with digitonin according to the method of Windaus, while in the other this was effected by saponification with freshly prepared sodium alcoholate. The difference between the two determinations gave the cholesterin made free from esters. Lecithin and phosphoric acid were also estimated. The highest cholesterin values were obtained in cases of diabetes, cholemia, and eclampsia, the lowest in cases of pernicious anemia, chlorosis, and inanition. In general, lecithin runs parallel with cholesterin; free cholesterin tends not to fall lower than 30 per cent. of the total cholesterin content of the blood. Bürger and Beumer were unable to confirm Rohmann's contention; in many cases the Wassermann was negative in sera unusually rich in lecithin, while in 2 cases of tabes and 1 of tertiary lues showing pronounced reactions, there were no cholesterin values obtained and lecithin was decreased. While believing that there is a definite relation between a positive Wassermann reaction and lipoids in the blood, Bürger and Beumer contend that this consists of something more than a mere increase in the two components under discussion. The exact significance of the numerous lipoids will continue to be a matter of speculation so long as we remain in ignorance of their genesis.

Quantitative Estimation of Urates in the Blood.—According to ZIEGLER (*Münch. med. Woch.*, 1913, lx, 1083) there have been two sources of error which may be held accountable for the failure of methods hitherto used to estimate the content of the blood serum in urates: (1) No method of protein removal gets rid of all the nitrogen; the so-called "rest nitrogen" results in uric acid determinations constantly higher than they should be; (2) deproteidization, moreover, removes a not inconsiderable portion of the uric acid present; (3) all methods have required relatively large amounts of blood and considerable time. To meet these defects Ziegler endeavored to discover a way of throwing down the uric acid while leaving the proteins in solution. The method is based upon the fact that copper sulphate forms a compound with uric acid, urates, and purins in general, which is insoluble in water; experiments showed that this compound remains quantitatively insoluble in the presence of a known concentration of NaOH. To perform the test, the following solutions are necessary: (1) NaOH, 4 per cent. solution; (2) $NaHCO_3$, 5 per cent. solution; (3) Neutral sodium sulphate, 3.5 per cent. solution; (4) $CuSO_4$, 2.5 per cent. solution; (5) A standardized solution of K_2MnO_4. Into a 200 c.c. Ehrlenmeyer flask containing 10 c.c. of clear serum, one adds 10 c.c. of solution 1, 20 c.c. of solution 2, and 10 c.c. of solution 3, and 20 c.c. of distilled water, in the order given. To the resulting mixture, one adds, while shaking, 10 c.c. of solution

4, from a pipette; a clear blue-violet solution results. Pour into an evaporating dish and boil until about one-third of the original volume has gone, at which time a gray-white precipitate comes down. Pour into a centrifuge tube, washing the evaporating dish well, and centrifuge at high speed, draw off the clear blue superwatered fluid, mix the precipitate well with water, centrifuge, and repeat until the fluid remains absolutely clear, colorless, and incapable of producing foam when shaken, this being a trustworthy test for the absence of protein. The sediment, now colloid free, is dissolved in 10 c.c. of concentrated H_2SO_4, and the uric acid determined by titrating with a solution of K_2MnO_4. It may be best to add a known amount of uric acid and, say, 0.01 gram, and titrate the difference. The serum used must be fresh, preferably sterile, and absolutely free from blood. The method will detect 0.005 to 0.025 gram of uric acid per 10 c.c. of serum, is relatively simple, and requires only an hour's time.

Addison's Disease.—Lowy (*Deutsch. Archiv f. klin. Med.*, 1913, cx, 373) presents a case of Addison's disease, diagnosticated clinically by reason of the marked pigmentation, myasthenia, diarrhea, emaciation, hypothermia, and low blood pressure, these symptoms occurring in association with rapid mental deterioration in a man, aged twenty-one years, who had previously been of more than average intelligence. Tuberculin tests were negative; there was no marked anemia, but a lymphocytosis of 33 per cent., and a mild grade of eosinophilia. At autopsy the interesting findings were, first the complete absence of the specific cellular elements of the cortex of both adrenals, which were composed entirely of medullary parenchyma and second the existence of a well-developed status thymicolymphaticus. Hedinger had previously called attention to the fact that in 15 cases of Addison's disease 7 showed the existence of a status thymicolymphaticus, while in 5 others there was pronounced lymphatic hyperplasia, and he expressed the idea first advanced by Wiesel that in these cases the normal balance between the lymphatic glands and chromaffin system had been disturbed through deficiency in the latter, to which was to be ascribed both the glandular hyperplasia and the various manifestations of Addison's disease. This theory was opposed to that which assumes that the cause of Addison's disease is to be found in the cortex of the adrenals; it has, moreover, been shown experimentally in animals that the adrenal cortex is necessary for life, a finding apparently confirmed in this case. The persistently low blood pressure, despite the apparent integrity of the adrenalin-producing cells, leads to the conjecture as to whether or not the thymus may have been responsible, Mohr having shown that thymus extracts are capable of producing tachycardia, asthenia, and low vascular tonus. Moreover, the embryological relationship between the "interrenal" system and the brain may in some way be turned to account for the pronounced mental changes observed in this case. Clinically the frequency with which Addison's disease is accompanied by a status lymphaticus should make one very careful to avoid any procedure apt to induce psychic disturbances, and a sudden lethal result. The relatively characteristic blood picture of Addison's disease finds reasonable explanation in the coincident glandular hypertrophy and recently

Weidenreich has shown that the thymus itself may be a source not only of lymphoid elements, but also of the granular cells and eosinophiles in particular.

The Irritative Effects of Ascaris on the Intestines of Man.—J. C. HUBER (*Münch. med. Woch.*, 1912, lix, 2669) reports a noteworthy case of ascaris infection. The patient, a boy, aged thirteen years, had suffered for two years from periodic attacks of pain in the right iliac fossa. Every two weeks or so, ascarides were passed with the stools. Huber saw the patient suffering with sharp pains in the right iliac fossa and vomiting. His temperature was 37.6, pulse 90. There was tenderness at McBurney's point and diminished resonance in the right iliac fossa. No mass was palpable. Appendicitis was diagnosticated and laparotomy performed. A moderate amount (50 to 510 c.c.) of free serous fluid was found on opening the abdomen. The appendix was perfectly normal in appearance. The ileum, however, for a distance of about 20 cm. showed a reddened serosa and plainly dilated lymph channels in the subserous layers. This extended to within 8 to 10 cm. of the ileocecal valve. In the mesentery of the congested part of the gut moderate swelling of the glands was visible and palpable. In the congested part and just above it one could feel worm-like bodies, evidently ascarides. Four days after the operation, seventeen ascarides were passed spontaneously. After administering santonin and calomel, forth-nine more worms were obtained. Huber suspects that such attacks as his patient sufferend from are not rare in ascaris infections, though the lesions may not always be so evident. The possibility should be considered, especially in patients known to be infected with Ascaris lumbricoides.

Superpermeability in Nephritis.—BAETJER, during the study of renal function in the various clinical types of nephritis (*Arch. Int. Med.*, 1913, xi, 593) was impressed with a certain peculiarity common to 4 cases, namely a supranormal excretion of some of the substances employed. All were outspoken clinical cases of chronic nephritis with edema and large content of albumin in the urine. In 3 of them the phthalein elimination was well above normal, 83 to 90 per cent., for two hours. The lactose test showed the same tendency—in one and two hours, in 2 of the cases, a marked increase in rapidity of excretion. In 2 cases there was a definite delay in the elimination of potassium iodide, sixty-eight and seventy-two hours. But in common to all was the impaired salt elimination, the one test which gave evidence of functional renal impairment in these cases. The association was of an impaired sodium chloride elimination with a supranormal excretion of lactose and phthalein. Baetjer believes that there may exist in some types of nephritis a stage in which the kidney is hyperpermeable, at least to some substances used for functional tests, with an elective impermeability for chlorides. This fact emphasizes the need of studying renal function from the standpoint of a considerable series of functional tests rather than to draw conclusions from the excretion of any one drug. Similar observations, as Baetjer points out, have been made as to the elimination of other coloring matters, notably by Bard, Bernard, and Castaigne, in connection with methylene blue.

SURGERY

UNDER THE CHARGE OF

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Operation upon Paralytic Feet.—MÜLLER (*Zentralbl. f. Chir.*, 1913, xl, 312) presents an operation for paralytic talipes calcaneus, which is indicated in those cases in which the gastrocnemius and soleus are paralyzed and the other muscles on the posterior side of the leg are preserved. As a substitute for the calf muscles, he takes on the inner side the flexor longus hallucis and on the outer side the peroneus brevis. A longitudinal incision, extending from one side of the limb to the other, is made between the tibia and fibula in front and the tendo-Achilles behind, and extending to the junction of the lateral surface of the tuberosity of the calcaneum and the posterior surface. Above, the incision is deepened to the flexor longus hallucis and peroneus brevis and below to the bony surface of the calcaneum. The latter is denuded of its fibroperiosteal covering and two small holes are drilled transversely through the tuberosity, one close above the other, and both very close to the posterior surface of the bone. Another incision is made along the external border of the foot to expose the tendon of the peroneus brevis which is then separated from its insertion to the fifth metatarsal bone. A fourth incision along the inner border of the foot exposes the tendon of the extensor longus hallucis, so that it can be divided in the middle of the sole of the foot. It is easily followed by passing a grooved director along its sheath from the inner side of the first double or through-and-through incision. The ends of the two divided tendson are brought, one out of each side of the first incision, and each is passed through one of the transverse canals in the tuberosity of the os calcis, so that the tendon of the flexor longus hallucis passes into the mouth of one canal and out of its external opening, and that of the peroneus brevis in the reverse direction through the other bony canal. The end of each tendon is then clamped with a forceps, and while the foot is strongly flexed in the plantar direction, the ends of the tendons are bound together. The two muscles then form a two-headed muscle inserted into the tuberosity of the os calcis. The tendo-Achilles is now shortened so that it will help mechanically to hold up the heel. The foot is kept in strong plantar flexion for four or five weeks, in a plaster cast. After the csat is removed, the foot is gradually brought to a right-angle position by exercises. Gradually plantar flexion is acquired,

so that in walking the anterior part of the foot is on the ground and the heel is raised. While not normal, walking becomes not much removed from normal. Müller objects to the usual arthrodesis of the ankle-joint in paralysis of the muscles of the foot and prefers arthrodesis of the astragalotarsal joint. The posterior part of the foot, by this operation, acquires firmness because the astragalus, calcaneus, scaphoid, and cuboid are bound together in one bony mass. The necessary flexion and extension of the ankle-joint are preserved, while all lateral movements are excluded.

Experimental Ligation of the Portal Vein; Its Application to the Treatment of Suppurative Pylephlebitis.—NEUHOFF (*Surg., Gynec., and Obstet.*, 1913, xvi, 481) says that the fact that no surgery of the portal vein has as yet developed appears to depend upon the results of animal experimental studies. He made an experimental study, comparing his results with those of other workers, and concludes that experimental complete ligation of the portal vein is immediately fatal. Death results from shock. Apparently normal life is compatible with complete occlusion of the portal vein, if gradually induced. This is true for the human being and the experiment. In the latter, gradual obliteration of the lumen can be successfully induced in a very brief period. The liver remains practically normal with complete occlusion of the portal vein existing for a short time (experimentally), and for very prolonged periods (clinically). The reason for this lies chiefly in the development of a hepatoportal circulation. The latter is demonstrable clinically and experimentally. In the experiment the hepatoportal circulation appears to develop regularly in the gastrohepatic omentum. An active treatment of suppurative pyelephlebitis is suggested on the basis of his summarized results. Ligation of the portal vein, with the modifications embodied in the paper, is the treatment that is advocated. The operation is worthy of a trial in an attempt to improve the results of an affection so regularly fatal.

Studies Concerning the Comparative Value of Non-pedunculated Flaps of Omentum, Peritoneum, and Mesentery, for the Reinforcement of Sutures.—SASAKI (*Deut. Zschr. f. Chir.*, 1913, cxiii, 62) says that peritoneal or mesenteric flaps are of substantial value for suture insufficiency in all abdominal operations. Omental flaps, on the other hand, are not deserving of much attention. The first two can take the place of the Lembert seromuscular suture, the last cannot. The striking difference in the results of the employment of these three kinds of flaps, depends chiefly upon the presence or absence in the flaps of the network of elastic tissue. The chief effect of this elastic tissue lies in the fact that with it the flaps can adapt themselves closely to the underlying layer and in the fact that the specific elasticity presents an unbroken resistance to the internal pressure of the gastrointestinal tube. The healing process can then go on favorably. Omental flaps do not favor these results because of the irregularity of its structure, its abundance of fat, the difficulty with which it applies itself, and its greater mass. Unfavorable conditions accompanied their employment, as contraction or adhesion of the flaps, with often produced restriction of the passage of the intestinal contents. The essentials

for healing, whether it concerns a double or single row of sutures, consists in the adhesion and growth of the apposed serous surfaces and the inner surface of the flap applied to the intestinal serosa, which with time organizes and is finally changed into cicatricial tissue. The healing, while completed by the regeneration process, is reinforced by the covering of the defect by endothelium. This endothelial covering is, unconditionally, dependent upon the vitality of the flap. Therefore, autoplasty gives the best results. Homoioplastic peritoneal flaps may also succeed unless necrosis occurs. Their permanent preservation, however, is very questionable. They appear to live until the defect is covered by mucous membrane. The use of a hernial sac from another individual may prove practical. When perforation of the omental flap was observed it occurred as a rule in the middle of the applied flap. The kind of suture, whether interrupted or continuous, had no influence on the perforation. One may often leave a peritoneal defect, because the endothelium can cover it from the surrounding part, after some time. In order to prevent adhesions, the defect may be closed by sutures. The flap may be employed as a prophylactic measure, when the stomach or intestinal suture cannot be relied on, when there is strong tension on the suture or the serosa is defective, and in any circumstances where such postoperative danger exists. It is also useful when there is a loss of substance after separation of adhesions, and with reserve it may be recommended in gastric and duodenal ulcers.

Function Tests in Connection with Transplanted Kidneys.—LOBENHOFFER (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1913, xxvi, 197) says that many experimental studies have been made from the anatomical as well as the physiological standpoints, to clear up the many questions concerned with the innervation of the kidneys. The purpose of his investigations was to study the manifestations of life of the transplanted kidneys in relation to our present knowledge. That such a kidney could supply the body with its normal function was known, but whether it could meet increased demands had not been studied. One may be deterred from undertaking further experiments on an animal on which a successful transplanation and nephrectomy have been done, because of the fear of killing it. The histological examination showed that the successfully transplanted kidney possessed, in a normal manner, the most delicate and sensitive structures in which lay the power of function. When the secreting cells lost their activity, the granules disappeared before anything else. For a permanent normal secretion the proper proportion of the normal constituents must be preserved and for this the nervous influence is necessary. The experiments sought to test the functional capacity of the tubular and vascular portions of the kidney. The investigations show that there was no considerable deviation from the normal in the activity of the transplanted kidney. The elimination of water and saline solution and the effect of foreign substances like milk sugar and phloridzin were tested. Since the experiments were carried out only on healthy animals which lived a long time in complete health, the conclusion is justified that the other functions of the kidney are performed in a proper manner. One may conclude that the successfully transplanted kidney

will meet not only all normal demands but those greater than normal. The normal urine secreted during diuresis caused by hydremia gives perfect proof that the vascular system of the transplanted kidney is complete. The work of the vessels is dependent upon the contractile elements and this again can only be due to the nervous influence. Since every nerve impulse to the transplanted kidney is cut off, the intrarenal plexus must be so far independent that it alone must exercise every necessary automatic impulse for the work of the kidney. This seems indisputable and is to be explained by the physiology. It shows that the nerve branches entering at the hilum give no specific secretory branches to the epithelium, since in a transplanted kidney the epithelial function could not be normal. At the present time, however, it would not be justifiable to conclude that the secretory filaments must come from the intrarenal plexus. Our knowledge of the nerve influence upon secretion is not yet definite enough to permit one to drawing binding conclusions. The Eckhard theory of the existence of a secretory centre for the kidney in the spinal cord cannot be wholly right. The branches to the kidney from the spinal cord and sympathetic must play a subordinate part. They probably interpose a regulating influence. There are probably other branches upon which the task falls to convey impulses centripetally and to cause reflex effects in other organs.

Concerning Immunity against Pancreatic Necrosis.—JOSEPH and PRINGSHEIM (*Mitt. a. d. Grenzegeb. d. Med. u. Chir.*, 1913, xxvi, 290) say that the experimental work that has been done during the past ten years on pancreatic and fat necrosis has been concerned chiefly with two points. In the first place the workers have attempted to produce in animals characteristic pancreatic and fat necrosis, with the object of obtaining light on the origin of the local affection. In the second place the efforts have been directed toward learning the cause of the severe, mostly fatal, general symptoms and thus drawing nearer to an effective method of combating them. They conducted a series of experiments with these ends in view and believe that they have contributed as much to the solution of the pathogenesis as have the recent investigations of Fischler. Fischler found that an animal with an Eck fistula (between the portal vein and inferior cava) showed after death all kinds of degeneration of the liver parenchyma in severe grade, and frequently died with severe symptoms of auto-intoxication. In these foci of degeneration he demonstrated the products of fat splitting by steapsin and brought them into relation with mild pancreatic lesions from operation and fat necrosis. In this way a causal relationship was constructed between pancreatic necrosis, loss of function of the liver from an Eck fistula, and fatal antointoxication. As Guleke and von Bergmann had already shown, a preliminary subcutaneous treatment of dogs with trypsin, provides protection not only against the toxic effect of larger doses of trypsin, but also against the toxic effect of pancreatic substance introduced into the peritoneal cavity. Their experiments show that the immunity is provided only against a certain amount of the pancreatic substance in the peritoneal cavity. In order to provide further protection, the embedding of the pancreatic substance into the peritoneal cavity must be preceded

by an immunization with increasing doses. These experiments furnish a further support for the view that the toxic effect of the necrotic pancreas does not depend alone upon the toxic effects of its proteolytic ferment. The immunity obtained by preliminary treatment with trypsin and pancreatic substance cannot be transferred to other animals.

THERAPEUTICS

UNDER THE CHARGE OF

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The Interpretation of the Results of the Wassermann Test.—CRAIG (*Jour. Amer. Med. Assoc.*, 1913, lx, 565) gives his interpretation of the results of the Wassermann test after antiluetic treatment. The conclusions regarding the interpretation of the Wassermann test were derived from the study of 10,000 tests made in the Army Laboratory in Washington. The total number of individuals tested has been 5216, while 4784 reëxaminations were made generally as a control of the treatment. In the vast majority of the 4784 reëxaminations the test was made for the purpose of controlling treatment with salvarsan, mercurials, or both. The results have demonstrated the great value of the Wassermann reaction as an index of the efficiency of treatment and it has been possible to trace the gradual disappearance of the reaction in treated cases and its reappearance in those instances in which further treatment was required. The use of the reaction in this manner has made possible the intelligent administration of both salvarsan and mercury and every patient suffering from syphilis should have the treatment controlled by Wassermann tests made at intervals of at least two months. Only in this way can justice be done the patient and the specific treatment of syphilis be conducted in an adequate and scientific manner. The occurrence of a double-plus or plus reaction following treatment should always be interpreted as meaning that more treatment is necessary. Granted that as most observers believe, the presence of a positive Wassermann reaction means the presence of living spirochetes, it is evident that when such a result is obtained the patient cannot be considered as cured, even though symptoms may have been absent for months or even years. A plus-minus reaction after treatment, provided it is obtained on repeated examinations, should also be considered as an indication for more treatment, but when such a reaction is obtained treatment should not be given until the test has been repeated, unless symptoms are present. A negative reaction after treatment is of no value as an evidence of cure unless it remains negative for at least a year and no symptoms have developed meanwhile. The limit of a year is arbitrary and founded on the experience in controlling the treatment in hundreds

of cases of syphilis. Only one relapse was observed, in a patient whose Wassermann reaction has remained negative for a year after the cessation of treatment. A luetin test should also be made, even though the Wassermann test is negative.

Fatal Result Following Benzol Treatment of Leukemia.—JESPERSEN (*Deutsch. med. Woch.*, 1913, xxxix, 1300) reports a case of myeloid leukemia treated by benzol in which the improvement at first was very marked. In the course of the first ten days of benzol treatment the leukocyte count fell from 250,000 to 61,000. This fall in the leukocytes was accompanied by a considerable improvement in the general condition without, however, an appreciable effect on the side of the liver or spleen. On the seventeenth day of treatment the red blood count had increased from 2,000,000 to 3,250,000, but on the following day a severe epistaxis occurred and the benzol was discontinued. The condition of the patient became very grave, the red blood cells falling below 2,000,000. After a benzol free period of twelve days benzol was again given in larger doses, up to 5 gm. a day, giving during the following thirty-two days a total amount of 97 gm. of the drug. There were no untoward symptoms and no evidence on the part of the urine of any toxic action. During this period marked improvement in the general condition occurred and the leukocyte count fell to 5,000 per c.c. The spleen and liver decreased markedly in size and the patient was cured so far as subjective symptoms were concerned. In a later note to the article Jespersen relates a rapid recurrence of all the symptoms. Ten days after the count of 5,000 the leukocytes had risen to 300,000, the liver and spleen rapidly enlarged, the fever returned, severe epistaxis and uncontrollable vomiting developed and the patient died twenty-three days after the apparent cure. During this recurrence benzol was again given systematically except during the last ten days when the vomiting did not permit of the remedy. The blood count on the last day showed a rise of leukocytes to 750,000 and the reds showed changes resembling those of pernicious anemia. Jespersen does not believe that these symptoms were due to benzol poisoning but that they were due to a recurrence of the leukemia in a more acute form.

Diuretics in Cardiac Disease.—HIRSCHFELDER (*Jour. Amer. Med. Assoc.*, 1913, lxi, 340) says that in considering the subject of diuretics in cardiac disease it is essential to have some tentative idea of the forms of cardiac disease in which it is desirable to resort to diuretics to all; secondly, that we form a clear idea of the manner in which the lesion of the heart effects the action of the kidney; and thirdly, that we consider the mode of action by virtue of which the particular diuretic drugs under consideration may be expected to remedy these disturbed conditions. Hirschfelder mentions five forms of disease of the circulation in which resorting to diuretic measures might be advisable: (1) infective endocarditis; (2) arteriosclerosis with periodic attacks of the various disturbances associated with localized arteriosclerosis, vertigo, headaches, transitory cardiac asthma or pulmonary edema, angina pectoris, and vasomotor crises; (3) chronic or paroxysmal hypertension without edema; (4) acute cardiac overstrain, and (5)

broken systemic compensation with chronic passive congestion and edema with or without general anasarca, ascites, hydrothorax, or hydropericardium, arising from myocardial weakness, valvular insufficiency, or adherent pericardium. Acute and chronic infective endocarditis is associated with a scanty urine with albumin and red blood cells, but this is due to the presence of a true infective glomerulonephritis, and should accordingly be treated as a primary nephritis rather than as a primary heart disease. In the group of arteriosclerosis and of chronic hypertension as von Noorden has shown, it is better to spare the arteries and kidneys from overwork by light diet and restriction of salt and water than to remove these substances from the system with diuretics. In acute cardiac overstrain, the diminution of urine is of transitory duration and clears up when the strain is removed. The chief condition in which active intervention to induce diuresis is advisable is in the group of cases of broken compensation with chronic passive congestion. The functional power of the kidney in passive congestion is extremely variable and may be easily determined by the different functional tests. It is possible to determine by these tests if the tubules or the glomeruli are chiefly at fault and to select the remedies most suitable. The diuretic action of digitalis depends on its action in the circulation, the velocity of blood flow, and the pulse pressure. If the diminished urine output is due to failure of the filtration through the glomeruli it is possible to increase filtration through glomeruli by digitalis preparations. This action is marked in cases of cardiac irregularity and especially in patients with auricular fibrillation. In using digitalis it is important to obtain a preparation which has been standardized physiologically in order to secure sufficient dosage, but aside from this Hirschfelder does not think there is any essential differing in the choice of the preparation to be used. Digitalis infusion probably contains more digitoxin than the other preparations, but he does not think a good infusion is more efficacious than an equally good tincture, whereas, on the other hand, infusions are more subject to variation and spoiling. Strophanthin in doses of from 0.5 to 1 mg. injected intravenously or intramuscularly is also an excellent diuretic. Other members of the digitalis group—squill, convallaria, adonis vernalis, hellebore, etc., are in general inferior to digitalis. Where a more powerful diuretic action is desired than is afforded by digitalis, the diuretics of the purin group are indicated, such as caffein, theobromin, theophyllin or theocin which act by dilating the renal vessels and by direct action on the epithelium. Of this group the most convenient form of all is the water-soluble acet-theocin sodium in doses of about three grains three times a day; it not only gives greater diuresis, but may also cause diuresis in cases in which theobromin sodium salicylate evoked no response whatever. Members of this group should be used with caution since they may actually diminish renal secretion when the kidney cells are much damaged. It is necessary to make a preliminary phthalein test to determine in any given case the exact extent to which the renal epithelium is injured. If the phthalein excretion is low—30 per cent. or less in two hours—we know at once that we are somewhere near the point at which theocin might injure the renal epithelium; and it will be better to rely on the digitalis and try to improve the circulation before trying to stimulate the kidney.

If the general circulation improves, the function of the renal epithelium will return very rapidly to nearly normal, and then one need not be afraid of acting on it with these powerful diuretics. Therefore, we should aim first to improve the circulation with digitalis and leave the removal of the edema for the administration of caffein diuretics. The good effects of calomel in cardiac disease is testified to by its long empirical use. Calomel acts particularly on the tubules, and tends to increase the excretion of sodium chloride more than the total volume of urine. However, it must not be forgotten that calomel acts on the kidney by being converted to mercuric chloride and that any excess may give rise to a bichloride nephritis which affects chiefly the tubules. It is particularly dangerous, therefore, in cases in which the renal epithelium is already badly damaged, and the precaution of a phthalein test is therefore doubly advisable. There are many purely physical measures that affect the excreting power of the kidney such as removal of ascitic fluid by paracentesis, tapping a hydrothorax or a venesection. After venesection, the circulation through the kidney is probably accelerated by a decrease of blood viscosity. Hot packs or poultices over the kidneys and intestinal irrigations may also cause further dilatation of the kidney vessels from heat alone, and thus brings on diuresis. Rest to the kidney is secured by dietetic measures, such as the Karell diet, limitation of water intake, limiting the ingestion of salt, etc. In general Hirschfelder says one should aim first to know the exact state of the kidneys; second, to improve the circulation with digitalis and to spare it with the Karell diet, and thirdly to resort to theocin or the saline diuretics to relieve edema if the renal epithelium is not severely injured.

PEDIATRICS

UNDER THE CHARGE OF

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Cyclic Vomiting in Children.—HUGH T. ASHBY (*Practitioner*, 1913, xci, 53) gives this following description of cyclic vomiting. The chief feature is incessant vomiting lasting from twelve hours to several days. The attacks come on without any warning during a period of good health. Children subject to them are nearly always of a neurotic stock. The diagnosis is often difficult where no history of a previous attack can be obtained. Other signs of disease are usually lacking. The absence of much rise in temperature, quick pulse, sweetish smell of the breath, and the presence of acetone and diacetic acid in the urine will aid in forming a definite diagnosis. As many other diseases of childhood begin with vomiting these must be excluded. If the vomiting continues more than twenty-four hours without any other signs appearing it is usually cyclic vomiting. The prognosis is generally

good although the condition is accompanied by much exhaustion and a run down condition. The condition seems to be allied to delayed chloroform poisoning, although the results are not so fatal. The attacks may begin soon after the twelfth month. They tend to become less frequent and severe and usually die out by the time of puberty. Intervals between the attacks vary from three or four weeks to once or twice a year. The chief pathological feature determined is the presence during the attacks of an acidosis, or acetone and diacetic acid in the urine and breath. The most plausible theory is that there is an intestinal toxemia due to disturbance of the liver function causing the presence of acetone and diacetic acid. Postmortem findings show fatty degeneration in most of the internal organs similar to that of chloroform poisoning. Mellanby found creatin excreted in the urine only under such conditions, the amount increasing as the attack came on. On the theory that the carbohydrates are absent or not utilizable in this condition the treatment is to give large quantities of sugar by mouth during the attacks, in the form of glucose and soda-water. Glucose is also given by rectum in large quantities. The intestine is kept free by enemas. This treatment gives better results than sodium bicarbonate in large doses.

The Diagnosis of Tuberculous, Bronchial, and Mediastinal Glands.—J. H. ELLIOTT (*Canadian Med. Assoc. Jour.*, 1913, iii, 679) says that practically all children with tuberculosis have involvement of these glands. In European cities over half of the children from the fourth to the eleventh year are tuberculous. In 920 children dead from all causes in Paris, 538 showed gross tuberculous lesions at autopsy. All stages of tuberculous disease affect the bronchial glands just as they do the cervical glands.

The constitutional symptoms are those long known under the name scrofula. Pressure symptoms may include those following pressure on the trachea or bronchus, the aorta and bloodvessels of the mediastinum, or the pneumogastric and other nerves. Rupture of a caseating gland may occur into a bronchus, the trachea, the lung, or into a bloodvessel. Toxic symptoms show malaise, anorexia, anemia, and loss of weight. Pressure symptoms include cough, dyspnea, asthma, and bronchitis. Physical signs include unilateral dilated veins, slight puffiness of the face and eyelids, unequal expansion of the apices, and unilateral or bilateral flattening or retraction. Tenderness over the upper thoracic spines, especially the fifth, and tenderness over the manubrium is suggestive. Dulness on percussion over the intercostal spaces, especially the first and second on the right side is valuable, denoting enlargement of the anterior mediastinal group. Dulness on percussion below the fourth thoracic vertebra is not normal and suggests mediastinal tumor. There may be interscapular dulness from the second to the fifth dorsal spines. Bronchial breathing and bronchophonic voice sounds may be found over these areas of paravertebral dulness. The *x*-rays are extremely valuable in diagnosis as they show up appreciable enlargement of glands and the degree of invasion of the lungs. Of the tuberculin tests the Von Pirquet is the most useful. However, a negative reaction does not exclude tuberculosis. Elliot thinks it may be absent in some quiescent closed cases, in some advanced active cases, and in so-called refractory cases.

Appendicitis in Children.—G. C. E. SIMPSON (*Brit. Jour. Child. Dis.*, 1913, x, 400) reports his conclusions on 34 cases of appendicitis in children. The general impression is that these cases are increasing of late years both in number and severity, and hospital records apparently bear this out. In 30 cases of Simpson's, fecal concretions were found in 18. The concretions appeared to determine the site of ulceration and gangrene. The cases in general showed a tendency to early perforation and gangrene; among the 30 cases only 3 showed the mischief still confined to the appendix at time of operation. General peritonitis was present in 13 cases and in 9 others there was spreading peritonitis. Of 12 cases under eight years all had perforated. Out of the 30 cases only six admitted of primary closure. Five cases died. Earlier recognition of the symptoms and earlier operation will prevent many of the deaths. In this series severe abdominal pain was an early symptom in all save one. Vomiting occurred in 25 cases, constipation was a prominent feature in 10 cases; pyrexia was absent on admission in only 2 cases. Marked tenderness and rigidity over the right iliac fossa were present in 28 cases. Diminished mobility of some part of the abdomen on respiration was marked in 20 cases. Attacks of vomiting and abdominal pain with elevation of temperature in children should demand a thorough examination by a physician, and the presence of any tenderness or rigidity in the right iliac fossa should at once demand the opinion of a surgeon. In all stages of acute appendicitis in children operation should follow immediately on diagnosis. The signs and symptoms may be slight, yet with very serious conditions in the abdomen.

OBSTETRICS

UNDER THE CHARGE OF

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Pregnancy Complicated by a Large Cyst of the Posterior Vaginal Wall.—FISCHER (*Monats. f. Geburts. u. Gynäk.*, 1912, xxxv, No. 4) reports the case of a multipara who came into spontaneous labor, and upon examination was found to have a large cyst of the posterior vaginal wall. The exact diagnosis of the condition occasioned some difficulty, labor ceased, and an attempt was made to deliver by forceps. During this attempt a rounded body was expelled from the vagina, which proved to be the cyst. The head was readily delivered so soon as the cyst had been removed. The cyst contained a yellowish fluid, and, upon examination, was found to be multiple, some of its compartments containing hair and yellowish material. This was composed of degenerated cells and fat. The wall of the cyst proved to be tissue resembling epidermis with papillary bodies. Hair bulbs were found in the epidermis.

Pregnancy Complicated by Prolapse of the Genital Organs.—Solomons (*Jour. of Obstet. and Gyn. of British Empire*, March, 1912) reports two cases of extensive prolapse of the genital organs complicating pregnancy. The first was a multipara whose prolapse was so extensive that she was obliged to remain in bed during a previous pregnancy. Later, she came to the hospital three months pregnant, and again pessaries failed to give her relief. She was then operated upon by colporrhaphy; amputation of the cervix, shortening of the uterosacral ligament; perineorrhaphy was extensive; posterior colporrhaphy, and the Alexander Adams operation. This was done at the fourth month, and the patient's pregnancy proceeded without interruption, terminating in spontaneous labor with the birth of a well-developed child. In the second case, a multipara, the uterus completely prolapsed at six weeks and could not be retained by pessaries. At four months the patient had severe pain, with a temperature of 104° F. The cervix was edematous, ulcerated, and prolapsed. A diagnosis of septic infection was made, and it was thought that the uterus should be emptied. The patient was given 20 c.c. of antistreptococcic serum, and a very hot vaginal douche, followed six hours later by the discharge of a three and a half months' decomposing fetus. The placenta was adherent and removed with difficulty. The patient recovered. Solomons has collected the results of pregnancy in 26 patients in whom the uterus had been sustained by a vaginal suspension for prolapse; 21 of the 26 patients considered themselves cured by the operation, and many had passed through pregnancy successfully, retroversion returning in but 2 cases.

Laceration of the Vagina During Labor.—Bjorkenheim (*Zentralbl. f. Gynäk.*, 1913, No. 8) from the clinic at Helsingbors reports the case of a multipara whose labor delayed so that the midwife in attendance called in a physician. The cervix was dilated, but the head was large and movable above the pelvic brim. The heart sounds were weak and irregular, and accordingly the forceps was applied. The instrument was removed and an attempt made to deliver by version, the midwife making strong pressure on the abdomen of the patient while the physician delivered the child. The head passed through the upper pelvis with great difficulty. There was fracture of the clavicle with dislocation of the cervical vertebra, and the child was dead born. Unfortunately, it was not weighed. In half an hour after the extraction of the child an effort was made to deliver the placenta by Credé's method. This failed, and the hand was introduced to remove the placenta, when the hand, following the cord, passed into a large cavity on the left side of the empty uterus. The placenta could not be found, but the hand passed through the opening into the abdomen among the intestines. The vagina was packed with gauze, and the patient brought by railway to the hospital. Upon admission, the general condition was fairly good, the patient was pale, but there was no fever, and the pulse was good. The umbilical cord was found passing to the left side of the vulva and thence through a large tear into the abdominal cavity. The placenta was very carefully drawn out by the cord, followed by dark blood. The patient was etherized, and abdominal section performed when the uterus was firmly contracted, but at the

side of the uterus there was a quantity of dark blood. In the space between the uterus and the bladder there was a tear in the peritoneum 10 cm. long, and the vagina was separated from the cervix through a distance of 6 cm., the opening communicating with the abdominal cavity. The parts were stitched together and a tampon of iodoform gauze placed in the parametrium through the vagina. The patient made, in the end, a good recovery, but this was complicated by pleurisy.

ZUBRZYCKI (*Zentralbl. f. Gynäk.*, 1913, No. 8) reports the case of a multipara in labor with strong pains, in whom the midwife discovered a tumor forming in the vulva. The physician who was summoned found, upon the left side of the vulva, a large elastic hematoma. Upon vaginal examination, it was observed that the tumor extended along the vaginal wall to the cervix, so that the lumen of the vagina was almost completely closed. The external os was dilated, the membranes ruptured, and the head of the child was in the pelvic cavity. During examination the tumor ruptured, discharging a mass of blood and blood clot. This was followed by very free hemorrhage. The child was immediately delivered by forceps, followed by the expulsion of the placenta, when the tumor was thoroughly irrigated, the bleeding vessels tied, and the cavity of the tumor drained with iodoform gauze. The patient's recovery was uninterrupted.

The reviewer, in a case in which a fruitless effort had been made to deliver by forceps, found a laceration of the vagina opening into the abdominal cavity sufficiently large to admit three fingers. The patient was delivered by the Porro operation, and the rent closed from above by a continuous catgut suture. Her recovery was uncomplicated, the torn vaginal tissue healing completely.

Pregnancy Complicated by Various Diseases.—In the *Annali di Ostetricia*, 1912, No. 4, PEZZINI and PIRANI report 27 cases of cholera complicating pregnancy. They find that pregnancy does not occasion any immunity against the cholera infection. The prognosis is not essentially altered by the pregnant condition, but becomes more grave the later in pregnancy cholera develops. The tendency to the interruption of pregnancy increases as pregnancy proceeds. The fetal mortality is very high, and the puerperal period does not seem to be greatly influenced by the disease. Where pregnancy is uninterrupted, and the patient survives cholera during the early months, the pregnancy may proceed to its normal termination.

An interesting case of echinococcus developing outside the peritoneum and behind the cervix is reported by GUSSAKOW (*Zentralbl. f. Gynäk.*, 1912, No. 28). The case had been mistaken by a physician for retroflexion of the pregnant uterus. The patient was kept under observation during pregnancy until labor developed, when she entered the hospital. The head of the child was above the entrance to the pelvic cavity, and the fetus in good condition. It was determined to open the posterior vaginal wall and endeavor to remove the tumor. Should this fail, abdominal section would be necessary. Upon incising the vagina, the tumor was opened and the characteristic echinococcus cysts removed. The tumor was reduced in size as much as possible, and labor proceeded with the mechanism characteristic of flat pelvis.

As labor pains were weak, three doses of pituitrin were administered during labor. The child was finally delivered by forceps, and although asphyxiated, recovered. The tumor cavity was packed with gauze, and the patient made a good recovery.

FRANZ (*Zentralbl. f. Gynäk.*, 1912, No. 28) has had good results in skin lesions occurring during pregnancy by the injection of a serum obtained from the blood of the umbilical cord. The patient was a primipara, aged nineteen years, who suffered from an eruption upon the skin of the abdomen, which itched violently, and spread upon the arms and legs. The lesions seemed to be multiple erythema with exudate; 20 c.c. of blood was taken from a vein, and 30 c.c. of serum two and one-half month's old, and obtained from the umbilical cord, was injected deeply into the right thigh. The temperature before and after the injection remained normal. The itching subsided when the eruption disappeared from the forearms. A fresh eruption appeared upon the left knee, and over other portions of the body characteristic spots developed. A second injection of 30 c.c. was given in the left thigh, followed by the disappearance of the exanthem from the abdomen and arms. The temperature and pulse remained normal. The eruption disappeared when labor developed with spontaneous birth and undisturbed recovery.

Glandular disease during pregnancy is the subject of a paper by RÜBSAMEN (*Archiv f. Gynäk.*, 1912, xcviii, No. 2). His first case was that of a primipara, aged sixteen years, with typical myxedema. Normal labor was followed by great improvement in the general condition, with a normal puerperal period. Thyroid extract seemed to be valuable in this case. A second patient was a primipara, aged thirty-two years, with cretinism, and contracted pelvis, delivered by section. The termination of pregnancy was followed by progressive improvement. The third case was a typical cretin, aged thirty-nine years. She was in the hospital for some time during her pregnancy, and showed great mental depression, with stupidity. The pelvis was highly contracted. After delivery by section, she improved very considerably. In four months after the operation, she was able to write plainly and was much better in general health. He gives the statistics of the clinic in Berne, where, among 718 patients, 34.2 per cent. had thyroid disease. He finds that after the classic operation on the thyroid, if this be done upon nulliparous patients, the tendency to the return of thyroid disease is less than if the patient had borne children before operation. He also describes, with photograph and *x*-ray illustrations, the case of a patient with substernal struma and twin pregnancy. The tumor was composed of two masses as large as a man's fist, with slight tremor in both hands, and some alteration in the eyes. The trachea and larynx were pressed upon by the tumor. Upon admission to the hospital, the patient's respiration was so labored that she could not lie down without difficulty. Upon coughing, the veins of the neck and chest became greatly distended. Viability was waited for, and the patient delivered as rapidly as possible by vaginal section, with lumbar anesthesia. It was found that twin fetuses were present, corresponding in development to the patient's menstrual history. The patient improved gradually after delivery.

GYNECOLOGY

UNDER THE CHARGE OF

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Palliative Treatment of Cervical Carcinoma.—An extremely simple form of treatment for inoperable cancer of the cervix, but one which is said to be extremely efficacious, is reported by BERCZELLER (*Zentl. f. Gyn.*, 1913, xxxvii, 852). It consists merely in the application to the cervix of powdered sugar; the cervix is exposed in a cylindrical glass speculum, and wiped dry, the speculum is then half filled with the sugar, which is kept in place by means of an iodoform gauze pack. The treatment may be repeated from once a day to once a week according to the severity of the symptoms. Berczeller has found that its adoption is followed by a rapid disappearance of offensive odor and discharge, with a reduction in the amount of bleeding; the surface of the tumor becomes dryer, and the mass is reduced in size. In addition to these local improvements, there is often noted a general picking up in the patient's condition, due to lessened obsorption of toxic products.

Hysterectomy by "Décollation Antérieure."—In cases of bilateral pyosalpinx, associated with extensive pelvic adhesions, the removal of the uterus by the method known as "décollation antérieure" is considered by BARNSBY (*Ann. mens. d'Obst. et de Gyn.*, 1913, ii, 449) "a truly marvellous operation." Orginated by Faure, this procedure is especially indicated in those cases in which, after opening the abdomen, one comes upon a solid conglomerate of omentum, intestines, uterus, tubes, and ovaries, all fused into an indistinguishable mass, completely filling Douglas' pouch, and rendering the posterior surface of the uterus entirely inaccessible. In such cases, often the only definite landmark obtainable is the anterior surface of the uterus, or a portion of it. After ligating and cutting the round ligaments, and freeing any omental or intestinal adhesions to the anterior surface of the uterus (but disregarding all others) until the cervix is reached, the operator clamps, ties, and cuts the uterine vessels, and *then* cuts through the cervix *from before backward*. After cauterization and closure of the remaining cervical stump, the body of the uterus is drawn strongly upward, the adhesions to its posterior wall being at the same time carefully liberated. It is now a comparatively easy matter to perform that part of the operation which at first appeared so difficult—the removal of the adnexa, for as the uterus, turned completely upside down, is pulled up, the adnexa gradually free themselves owing to the unfolding of the two layers of the broad ligaments which takes place, following the uterus in its ascent. This leaves the utero-ovarian pedicle free in the fingers, to be clamped and cut; the adnexal masses, thus released, are easily drawn out and freed from their superior and lateral adhesions. In exceptionally bad cases it may be necessary to insert

the hand back of the adnexal mass in order to liberate this, a simple procedure when the line of cleavage is followed along the anterior wall of Douglas' pouch. One of the chief advantages of this operation in Barnsby's opinion, is the fact that the uterine vessels are tied before any attempt has been made to free the inflammatory masses; thus, in the later stages there is no hemorrhage to obscure the field and hamper the operator, nor is there any necessity of placing one clamp after another in friable tissue, in which they do not hold. It is usually possible, Barnsby has found, to remove the largest pus tubes without rupture by this method, but if an opening is inadvertently made into an abscess cavity or into the rectum, the unbroken diaphragm of adhesions above protects the general peritoneal cavity from infection.

Menstrual Molimina in Healthy Women.—The frequency and severity of subjective disturbances associated with the menstrual function in the normal young woman of average health are subjects upon which much has been said and written, but often without much basis of actual definite data, since such information is as a rule exceedingly difficult to obtain. Of considerable interest, therefore, are some investigations of CHISHOLM (*Journ. Obst. and Gyn. Brit. Emp.*, 1913, xxiii, 288), who has analyzed the records of 500 healthy girls and young women, aged from ten to twenty years, which were obtained at the routine physical examination required by a certain school. The purpose of these investigations were to determine the amount of conscious disturbance coincident to menstruation, the nature of such disturbance, and if possible its cause. Only about 16 per cent. of the girls had any lasting irregularity following puberty; in all the others, the function became regular within a comparatively few months after its onset. In almost 59 per cent. no disturbance of any kind was admitted as occurring at the menstrual period, in 14 per cent. there was very slight, occasional pain, and in 19 per cent. fairly constantly recurring pain, but so slight as to be little more than discomfort. In only 8 per cent. of the cases was there severe pain at each period, and in less than 2 per cent. was this so severe as to incapacitate the patient for a time. In those cases where pain was present, and of sufficient definiteness to be localized, it occurred in about 75 per cent. in the abdomen, the next most frequent site being the back. A few of the girls complained of headache, and other symptoms of general metabolic disturbance, such as vomiting, general lassitude, and malaise; nervous irritability was conspicuous by its absence. The local pain complained of was either aching or colicky in character, the former occurring especially frequently in a central position just below the umbilicus, and probably resulting from uterine congestion. Chisholm does not believe that the majority of menstrual disturbances are due to developmental abnormalities, since in many instances pain develops only some years after the commencement of menstruation, and must therefore be due to some subsequently developing condition. In only a little over 6 per cent. of the cases was there an undue profuseness of the flow. These girls did not appear to be below the average in general health, and the condition was in most instances relieved by having the patient stay at home for the first few days of each period. Chisholm has found that while, on the whole, the best developed girls are least

likely to suffer from menstrual disturbances, there is no very marked difference in this respect. In her experience, menstrual disturbances are not appreciably increased by hard mental work when this is carried on under healthy conditions, with plenty of opportunity for exercise and recreation, and she therefore does not altogether agree with the commonly accepted opinion that girls should be subjected only to the lighest mental activity, or should be kept from school altogether, during the time of puberty.

Heliotherapy in Gynecology.—Aimes (*La Gynécologia*, 1913, xvii, 129) says that in certain gynecological conditions much good may be accomplished by so simple a measure as exposing the body to the rays of the sun. He recommends the "sun bath" especially in cases of quiescent genital tuberculosis, but it is of value also in certain cases of chronic pelvic inflammatory disease, and of metrorrhagia. The technique consists merely in the exposure of the entire nude body if possible, if not, of the abdomen and pelvis, to the direct rays of the sun, starting with one or two seances per day, of 5 minutes each, and gradually increasing this according to individual tolerance, until the patient can remain practically the entire day without discomfort. The head should always be well shaded. Aimes has found that as a rule patients who tan most quickly show the greatest amount of improvement. In addition to causing a general improvement in the bodily functions, increasing the appetite, reducing nervousness, and inducing restful sleep, the sun's rays appear to have a distinct antiphlogistic and hemostatic action, the cause of which has not as yet been determined. Often this form of treatment is advantageously combined with hydrotherapy.

OPHTHALMOLOGY

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The Central Light Sense and the Central Chromatic Sense in Chronic Glaucoma.—Beauvieux and Delorme (*Archiv. d'Ophthalmol.*, February, 1913, p. 93) have studied these perceptions in a considerable series of cases of chronic glaucoma. Such studies have heretofore yielded rather contradictory results, some holding the investigation of the light sense to be a valuable factor in diagnosis, while others regard failure of this sense as of common occurrence, being in fact a necessary accompaniment of lowered visual acuity or narrowing of the visual field from whatever cause. The study of the light sense includes two distinct factors: (1) the absolute or minimum perceptible,

(2) the differential, meaning thereby the minimum appreciable variation. Beauvieux and Delorme conclude that in chronic glaucoma the differential light sense is affected first; it is diminished at a time when the opthalmoscopic lesions are but little marked. Such diminution is quite independent of lowered visual acuity or narrowing of the visual field. It is, on the contrary, intimately linked to the state of the intra-ocular tension. Variations of the absolute light sense: this function becomes affected only in advanced chronic glaucoma when the disk is already cupped. Such alteration in the absolute light sense is intimately connected with the optic atrophy which accompanies glaucomatous excavation. It does not depend upon the acuity nor upon the visual field; neither is it influenced to an appreciable extent by subsequent regulation of the tension through treatment, inasmuch as the optic atrophy upon which it depends is a definite lesion. Modification of the color sense: the color sense is usually normal in all cases where the absolute light sense is intact. When optic atrophy has begun disturbances of color perception are not rare. Differential diagnosis: considerable diminution of the differential light sense with entire preservation of the absolute light sense has been found by Beauvieux and Delorme to occur besides in glaucoma only in papillary stasis (choked disk). In optic atrophy, the absolute light sense is affected first, the differential sense only suffers after the ophthalmoscopic lesions are clearly pronounced. Then also disturbances of the color sense become the rule. Prognosis: normal light sense, absolute and relative, indicate integrity of the fibers of the optic nerve. The prognosis is probably best in those cases where the differential light sense is raised after instillation of pilocarpin. It is also very favorable even if amelioration does not follow the use of miotics but comes on after (Lagrange's) operation. Beauvieux and Delorme are inclined to think that the prognosis should be reserved in cases where the alteration in the differential light sense persists even after the tension has become normal.

Treatment of Divergence by Overcorrecting Concave Lenses.—H. LANDOLT (*Klin. Montsbl. f. Augenhk.*, January, 1913, p. 47) has obtained cure in cases of both exotropia and exophoria by the use of overcorrecting concave lenses. In one case of alternating divergent strabismus of high degree with emmetropic refraction and full vision in each eye, double tenotomy with subsequent prismatic and stereoscopic exercises was unavailing. Concave lenses of 6D before each eye gave instant orthotropia. The divergent strabismus became transformed into insufficiency of convergence. The minus lenses were employed for daily exercise; finally binocular vision was reëstablished even when the lenses were omitted. In a second case of high degree of insufficiency of convergence in a myope of 2D in both eyes with full vision, correcting glasses combined with 4 degree prisms base had but slight effect upon the exophoria; −3.5D without prisms gave entire relief. Both of these patients were young as must necessarily be the case. Landolt explains this effect of overcorrecting concave glasses as a logical deduction from that of convex lenses in the relief of convergent squint: The stimulus to increased accomodation

calls forth an augmented impulse to convergence also. This effect, as well as the opposite in the case of convergent lenses, can be readily demonstrated by holding a concave lens before a youthful emmetropic eye; excessive convergence immediately takes place. The reporter observes that no ill effects need be apprehended from the use of such glasses, it having been demonstrated that myopia is not caused by the accommodation, and that with present-day views, more is to be feared from undercorrection than overcorrection of myopia.

Brawny Scleritis.—In 1907 Schlodtmann described from Fuch's clinic under the term "brawny infiltration of the sclera and conjunctiva" a type of anterior scleritis which presented distinctive clinical features. Since this publication histological findings in 11 additional cases have been published. Tuberculosis, syphilis, and rheumatism have on clinical grounds apparently been excluded as etiological factors, and the cause of the condition has remained obscure. VERHOEFF (*The Ophthalmoscope*, January, 1913, p. 2) reports a case which came to histological examination, in which a positive Wassermann reaction was obtained. He concludes that "Brawny Scleritis is a distinct type of scleritis, differing essentially in both its clinical and histological aspects from anterior Nodular Scleritis. Clinically, it is characterized by the advanced age at which it occurs (usually over sixty), its insidious onset and extremely chronic course, and the diffuse congestion and thickening of the sclera and episclera without the formation of definite nodules. The infiltrated recti tendons, however, may simulate sclerotic nodules. Ultimately, the anterior part of the sclera becomes involved around its entire circumference and the process also invades the cornea. Evidences of intra-ocular involvement, such as vitreous opacities and iritis, occur late and are relatively slight. Pain likewise does not occur until late. The intra-ocular pressure is normal or elevated. Both eyes are usually affected, although not always simultaneously, and the disease usually leads to blindness in one eye at least. Histologically, in the early stages there is a diffuse plasma cell infiltration of the sclera and episclera. Later, or possibly at the same time, the sclera becomes pervaded by granulation tissue, the plasma cell infiltration increases and involves by continuity, first, the anterior part of the choroid and ciliary body, and finally, the whole uvea. Necrosis of the granulation tissue takes place, showing itself as areas of purulent infiltration containing numerous endothelial phagocytes filled with fat, or as well marked caseation. Giant cells may or may not be numerous. Periarteritis and endarteritis are marked in the affected tissues. Even in the advanced stages, where there is intense infiltration of the ciliary body, there is no formation of cyclitic membrane. Separation of the retina ultimately occurs, due to exudation of serum from choroid. The character of the lesions in Brawny Scleritis strongly indicates a syphilitc origin for the affection. This is also indicated by a positive Wassermann reaction obtained in Verhoeff's case, but until such reactions have been obtained in a number of cases, or spirochetes have been demonstrated in the lesions, it cannot be regarded as absolutely established that Brawny Scleritis is a manifestation of syphilis."

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Fibrinemia.—J. O. WAKELIN BARRATT (*Jour. Path. and Bact.*, 1913, xvii, No. 3) has published an interesting article describing his attempts to find the cause of death when hemoglobin solution is injected into the blood stream. It has been known that a solution of hemoglobin from red blood cells of a rabbit, if injected in sufficient amount into the ear veins of another rabbit, would cause dyspnea, convulsions, and finally death. The fatal result is not supposed to be due to dissolved hemoglobin, but to substances derived from the stroma of the red blood cell. Morawitz, who some years ago advocated the transfusion of defibrinated blood in cases of anemia, recommended that such blood should be kept for some time before injection, so that the fibrin ferment might be modified to an inert substance; such precaution, nevertheless, was not always successful. It has been further observed that the fatal symptoms occur even if the serum was obtained from the animal in which the injection was made. Barratt first directed his attention to finding out if red blood cells laked by the addition of distilled water yielded thrombokinase, which he was able to answer in the affirmative. He was further able to determine that the thrombokinase thus supplied, comes almost if not entirely from the red blood cells; the solution of hemoglobin, therefore, whether in the form of laked red cells, or of supernascent liquid contains thrombokinase. If thrombokinase itself be injected, fibrin is separated slowly, which blocks the smaller bloodvessels, and can be found in the bloodvessels of the lungs; this can also be seen when thrombin is injected. The separation of fibrin in all cases is due to the action of thrombin, and according to the rapidity with which thrombin is formed, clotting occurs in the heart and the great bloodvessels, or in the capillaries, the latter being the case if the separation of fibrin occurs slowly. The symptoms produced appear to be entirely the result of mechanical interference with the circulation, and Barratt was able to find no evidence of a toxic effect produced by the fluid injected.

Secondary Infection in Pulmonary Tuberculosis.—AVERY and LYALL (*Jour. Med. Research.* 1913, xxviii, No. 1) deal with the subject of secondary infection and its importance in pulmonary tuberculosis. They point out that there are three schools whose opinions differ upon this subject. They first consider that mixed infection plays no essential part in the progress of the disease, a view held by v. Leyden, Straus, Fraenkel, and others; the second group, among which are to be found adherents of the Koch school, Cornet, and others, considers that the lesions and the more severe symptoms of pulmonary tuber-

culosis are due to the secondary and not to the primary infection; the third school, in which are Baldwin, Marmorek, and Römer, considers that the lesions and symptoms may be caused by the tubercle bacillus alone, but in many cases severe symptoms and unfavorable progress are due to secondary infection. Necessarily in such a division of opinion, it is essential to closely define terms, and it may be said that most observers consider that the organisms which are accidental incomers from the air are not properly to be considered as secondary infecting agents, unless they actually invade the blood or the tissues. Avery and Lyall point out that some of the Koch school have receded from their first position, being compelled to recognize that the tubercle bacillus alone is able to cause fever, and that destruction of lung tissue can be brought about without the assistance of secondary infection. Baldwin and Marmorek have shown the power of the tubercle bacillus to cause lesions quite unaided by any other microbe, but on the other hand, such lesions progress more rapidly and more dangerously in the presence of secondary infections. Avery and Lyall examined very carefully the sputum of 5 bronchiectasis cases, and of 15 cases of pulmonary tuberculosis, isolating and identifying the organisms present. The bacteria found differed so little from those reported by Hastings and Niles in non-tuberculous diseases of the respiratory tract, that they felt it impossible to draw useful inferences from this part of the investigation. They made blood cultures in 5 cases of bronchiectasis, and 110 cases of pulmonary tuberculosis, of which 38 were far advanced in the disease; in no case were they able to demonstrate a secondary bacteriemia.

Chemical and Serum Therapy in Pneumococcus Infections.—Engwer (*Zeit. f. Hygiene u. Infek.*, 1912, lxxiii, Heft 2) has experimented with infective doses of varying strength of pneumococcus, and attempted to meet the disease by combinations of chemical and serum therapy; he has attained a certain degree of success. He has used a solution in oil of ethylhydrocuprein and finds it effective in pneumococcus infection of the mouse and the guinea-pig; while with certain degrees of infection all the control animals died, he was able to save a certain number of animals by treatment. His best results were obtained by a combination of this chemical therapy with the usual serum therapy, although under certain circumstances the two appear to be antagonistic instead of mutually helpful. Throughout the experiments some animals were found to be poisoned by the chemical, and such fatal results appeared to be greater in cold weather. Engwer considers that the action of the drug depends upon the actual destruction of the pneumococci outside the cells rather than upon any action obtained by phagocytosis.

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